

## Antimicrobial Pigments

The present invention relates to antimicrobial pigments and their use in various applications, such as cosmetics, inks, lacquers or plastics.

5

Microbial contamination is an essential concern in our daily life, whether it concerns cosmetic products, surface areas in bathrooms, surgical instruments or wall paints. The usage of preservatives is a common method for preventing microbial contamination. However, the current trends show that organic preservatives are not well seen as such in view of regulatory affairs. Therefore, there is a real need of new harmless and compatible anti-microbial substances.

10

Silver is a known antimicrobial metal and in the past various proposals have been put forward for incorporation of silver in a composition for application. EP 0 190 504 discloses an antimicrobial composition which includes silver as the antimicrobial agent and a hydratable or hydrated oxide as a promoter to enhance the antimicrobial effect. Such compositions may be used to coat appliances such as catheters or may be incorporated in bone cements. Exemplary the hydratable or hydrated oxide is formed from element selected from silicon, titanium, aluminium or zinc.

15

20

EP 0 251 783 describes an antimicrobial composition comprising an antimicrobial silver compound, such as silver chloride or silver phosphate, deposited on a physiologically inert synthetic support material, such as oxides of titanium, aluminium or silicon in particulate form. The surface area of suitable support materials should be extended. The resulting antimicrobial composition can be dispersed in a polymeric material to prevent an antimicrobial contamination.

25

30

The combination of antibacterial activity and electrical conductivity is described in EP 0 427 858. An inorganic fine particle such as mica, alumina or titanium oxide is coated with an antibacterial metal - such as silver, copper, zinc or lead - and/or antibacterial metal compound. The  
5 resulting particles can be introduced into synthetic polymers thus obtaining antibacterial and electrically conducting polymers.

EP 0 677 989 discloses an antimicrobial powder composition comprising inorganic particles, such as the oxides of titanium, aluminium or zinc, mica  
10 or silica, having a primary surface coating of a metal or metal compound, such as silver, copper, silver oxide, silver halides, copper oxide, zinc silicate, zinc oxide or mixtures thereof, and a secondary coating providing a protective function, such as silica and alumina. The secondary coating functions as a barrier between the antimicrobial particle and a polymer  
15 matrix in which it may be incorporated. Furthermore, the secondary coating layer is believed to influence the rate at which the antimicrobial component diffuses from a dispersed particle into the polymer.

EP 0 665 004 discloses antimicrobial cosmetic pigments comprising  
20 inorganic cosmetic pigments, an amorphous glassy coating layer of metal oxide formed over the surface of said inorganic cosmetic pigment and antimicrobial metals or antimicrobial metal ions intercalated inside the lattice of said coating layer of metal oxides. By forming an additional layer onto the cosmetic pigment, the colour of the pigment changes. This is  
25 undesirable for the manufacturer of applications or formulations because he is restricted to the colours that can be achieved with pigments having the additional layer.

In all citations described above, the antimicrobial activity is introduced into  
30 the application system via a material having only an antimicrobial effect or additional layers alter the properties of the pigments.

Products used in our daily life normally have a broad variety of features. Special effects of the products are for example often combined with colour such as in cosmetics, plastics, paints etc. Each feature has to be introduced into the product by a separated compound or material. This complicates the production process and especially in the case of cosmetic or pharmaceutical products this can result in restrictions for the allowance of compositions. It is therefore useful to combine several features in one component of the composition. One basic feature is colour, in fact nearly all products of our daily life are coloured.

It is an object of the present invention to combine the general properties of pigments or fillers with an antimicrobial activity without significantly altering the properties of the pigments or fillers with respect to colour, chroma and tinting strength of the pigments or applications properties such as skin feeling in the case of fillers.

Surprisingly, it has been found that pigments according to the present invention can fulfil all the objectives cited above. Therefore, the present invention describes antimicrobial pigments, obtainable by agitating a suspension comprising one or more inorganic pigments and silver oxide as antimicrobial compound.

Antimicrobial pigments according to the present invention combine the antimicrobial activity with the properties of the pigments, such as, depending on the pigments used, broad variety of colours or even transparency, tinting strength, hiding power, interference effects or lustre. In the case of fillers as basis materials for the antimicrobial pigments for example the skin feeling remain unaltered during the manufacturing process. The combination of features as described above eases the manufacturing of formulations because the amount of preservatives, which have to be added to the formulation, can be reduced. If desired, the colour of the employed inorganic pigment and the antimicrobial pigment does not

show a visually noticeable difference. Furthermore, antimicrobial pigments according to the present invention show good application behaviour, such as dispersibility, chemical stability and skin feeling.

- 5 Antimicrobial pigments according to the present invention can have any known regular or irregular shape, for example the shape of platelets, spheres or needles. Preferably the antimicrobial pigments are platelet-shaped or spherical.
- 10 Antimicrobial pigments according to the present invention can be prepared on the basis of all known inorganic pigments or as fillers used pigments. Inorganic pigments in this sense comprise (according to DIN 55944) inorganic white pigments, inorganic coloured pigments, inorganic black pigments such as for example Carbon Black, effect pigments and luminous
- 15 pigments, but also magnesium carbonate, mica,  $\text{SiO}_2$ ,  $\text{TiO}_2$ , aluminium oxide, glass, micaceous iron oxide, oxidised graphite, aluminium oxide-coated graphite, basic lead carbonate, barium sulphate, chromium oxide or  $\text{MgO}$  can be used in the present invention.
- 20 Preferably used are pigments selected from the group of effect pigments. Examples of effect pigments are those based on substrates which can additionally be coated with one or more layers of  $\text{BiOCl}$  and/or transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals,
- 25 metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials. The substrate for the effect pigments is preferably platelet-shaped and is preferably selected from the group of natural or synthetic mica,  $\text{SiO}_2$ ,  $\text{TiO}_2$ ,  $\text{BiOCl}$ , aluminium oxide, glass, micaceous iron oxide, graphite, oxidised graphite, aluminium oxide-coated graphite, basic lead
- 30 carbonate, barium sulphate, chromium oxide,  $\text{BN}$ ,  $\text{MgO}$ , magnesium fluoride,  $\text{Si}_3\text{N}_4$  and/or metal. Examples for metals are aluminium, titanium, silver, copper, bronze, alloys or gold, preferably aluminium or titanium. The

metals can be passivated by inorganic treatment. Effect pigments with natural or synthetic mica,  $\text{SiO}_2$ ,  $\text{TiO}_2$ , iron oxide,  $\text{BiOCl}$ , aluminium oxide and/or glasses are especially preferred as substrates.

5 For the one or more layers of transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials all known materials can be selected. There are one or more layers of transparent, semitransparent or  
10 opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials can have a high refractive index ( $n > 1.8$ ) or a low refractive index ( $n \leq 1.8$ ). The metal oxides or metal oxide hydrates can be selected from any known  
15 metal oxide or metal oxide hydrate, such as for example  $\text{SiO}_2$ ,  $\text{Al}_2\text{O}_3$ ,  $\text{TiO}_2$ ,  $\text{ZnO}$ ,  $\text{ZrO}_2$ ,  $\text{Ce}_2\text{O}_3$ ,  $\text{Fe}_2\text{O}_3$ ,  $\text{Cr}_2\text{O}_3$ ,  $\text{SnO}_2$ , silicon oxide hydrate, aluminium oxide hydrate, titanium oxide hydrate and/or mixtures thereof, such as for example ilmenite or pseudobrookite. The metal can be selected from any known metal, such as for example chromium, molybdenum,  
20 aluminium, silver, platinum, nickel, copper, gold and/or alloys, preferably from aluminium and/or silver. An example for a metal fluoride is magnesium fluoride. As metal nitrides or metal oxynitrides for example the nitrides or oxynitrides of titanium, zirconium and/or tantalum can be used. Preferably the one or more layers consist of metal oxides, metal oxide  
25 hydrates, metals and/or metal fluorides, in particular metal oxides and metal oxide hydrates. Furthermore, the effect pigments can have multilayer compositions comprising materials with a high and a low refractive index. Antimicrobial pigments based on multilayer effect pigments are characterised through an intensive, glossy lustrous appearance and an angle-  
30 dependent interference colour. Preferably the one or more layers of  $\text{BiOCl}$  and/or transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides,

metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials are arranged as alternating layers of transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials or  $\text{BiOCl}$  with a refractive index  $n > 1.8$  and transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials with a refractive index  $n \leq 1.8$ , in particular as stack of two layers comprising one layer of a material with a high refractive index and one layer of a material with a low refractive index, whereas one or more of these stacks can be applied to the substrate. The sequence of the layers of the material with a high refractive and the material with the low refractive index can be adapted to the material of the substrate thus incorporating the substrate into the multilayer composition. Preferred examples for materials with a refractive index  $n > 1.8$  are titanium oxide, iron oxide, iron titanate, iron, chromium, silver and/or nickel, preferably titanium oxide, iron oxide, iron titanate. Preferred examples for materials with a refractive index  $n \leq 1.8$  are silicon oxide, silicon oxide hydrate, aluminium oxide, aluminium oxide hydrate, aluminium and/or magnesium fluoride. In another embodiment the transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials additionally may contain organic and/or inorganic colorants or elements as dopant. The absorption colour of the organic or inorganic colorant is combined with interference effects of the one or more layers of metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials thus producing pigments with special colour effects. Examples of organic colorants are azopigments, anthrachinonepigments, indigo- or

thioindigo derivatives, diketo-pyrrolo-pyrrol pigments, perylen pigments or phthalocyanin pigments. Carbon black, Prussian blue, Turnbells blue, Rinnmanns green, Thenards Blue and coloured metal oxide are only few examples of inorganic colorants, which can be introduced into the one or more layers. Yttrium or antimony can be used as dopant. Combinations of the materials mentioned above, for example mica platelets coated with fine particles of barium sulphate and a thin film of titanium dioxide are within the scope of the present invention. Antimicrobial pigments based on all these systems combine the absorption and interference colour of the pigments with an antimicrobial activity thus enhancing the applicability of the pigments. Usage of these antimicrobial pigments can result in the reduction of the content of preservatives added to formulations and applications, thus enabling the reduction of production costs and efforts necessary by the applicant to prevent the formulations and applications to be contaminated with microorganisms.

The outer layer of the effect pigments which can be used according to the present invention preferably comprises a transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxide, metal suboxide, metal oxide hydrate and/or mixture of these materials, most preferably a metal oxide or metal suboxide with a high refractive index. This outer layer can be additionally applied to the one or more layers or can be one of them. Preferably the outer layer is composed of  $\text{TiO}_2$ , titanium suboxides,  $\text{Fe}_2\text{O}_3$ ,  $\text{SnO}_2$ ,  $\text{ZnO}$ ,  $\text{ZrO}_2$ ,  $\text{Ce}_2\text{O}_3$ ,  $\text{CoO}$ ,  $\text{Co}_3\text{O}_4$ ,  $\text{V}_2\text{O}_5$ ,  $\text{Cr}_2\text{O}_3$  and/or mixtures thereof, such as for example ilmenite or pseudobrookite,  $\text{TiO}_2$  is in particular preferred.

Examples and embodiments of the above-mentioned materials and pigment compositions are for example described in Research Disclosure RD 471001 and RD 472005, whose specifications are herein incorporated by reference.

The mean diameter of platelet-shaped substrates and hence the resulting pigments can vary between 1 and 200  $\mu\text{m}$ , preferably 10 and 150  $\mu\text{m}$ . Depending on the desired application, the size of the pigments can accordingly optimised. The overall thickness of the pigments is in the range  
5 between 0.05 and 6  $\mu\text{m}$ , in particular between 0.1 and 4.5  $\mu\text{m}$ .

The thickness of the one or more layers of transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides,  
10 metal oxynitrides, metal fluorides and/or mixtures of these materials can vary between 3 and 300 nm, preferably between 20 and 200 nm. The thickness of the metal layers is preferably in the range of 4 to 50 nm. By adjusting the layer thickness the intensity of the absorption colour or the interference colours and angles can be tuned.

15 Depending on the material of the substrate and the thereon-coated layers, antimicrobial pigments with variable colour, hiding strength, lustre and angle-dependent colour impressions (optically variable pigments) are obtainable.

20 The preparation of above described layers can result from wet chemical treatment, from sol gel processes or by chemical or physical vapour deposition (CVD/PVD). After deposition, the resulting pigments can be dried or calcined.

25 Examples of effect pigments described here comprise pigments like Iridon<sup>®</sup>, Candurin<sup>®</sup>, Timiron<sup>®</sup>, Colorstream<sup>®</sup> and Xirallic<sup>®</sup> pigments from Merck KGaA, Mearlin<sup>®</sup> and Dynacolor<sup>®</sup> pigments from Engelhard Corp., Variochrom<sup>®</sup> and Paliochrom<sup>®</sup> pigments from BASF or Spectraflair<sup>®</sup>  
30 pigments from Flex Products.



In another preferred embodiment of the present invention the inorganic pigments comprise spherical particles of metal oxides, for example  $\text{SiO}_2$ ,  $\text{TiO}_2$ , aluminium oxide, glass,  $\text{MgO}$ , iron oxide but also  $\text{BiOCl}$ , magnesium carbonate, graphite, oxidised graphite, aluminium oxide-coated graphite, basic lead carbonate, barium sulphate, chromium oxide, BN, magnesium fluoride,  $\text{Si}_3\text{N}_4$  and/or metals. Preferably the spherical particles comprise  $\text{SiO}_2$ ,  $\text{TiO}_2$ ,  $\text{Al}_2\text{O}_3$ ,  $\text{ZnO}$ ,  $\text{Fe}_2\text{O}_3$ ,  $\text{FeO}$  and/or mixtures thereof. Furthermore, the spherical particles can be coated with one or more layers of transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials. The materials for the one or more layers of transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials can be selected from the ones described for the effect pigments.

Spherical capsules of materials described above encapsulating organic and/or inorganic compounds or materials are also suited in the sense of the definition of inorganic pigments applied here. The encapsulated compound or material can for example be selected for example from UV-filters. Capsules, which are to be used particularly preferably, have walls that can be obtained by a process for example described in the application WO 00/09652, WO 00/72806 and WO 00/71084. Preference is given here to capsules whose walls are made of silica gel.

In one embodiment of the present invention the spherical particles are coated with one or more layers of transparent, semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates, metals, metal nitrides, metal oxynitrides, metal fluorides and/or mixtures of these materials. Layers of transparent

semitransparent or opaque, selectively or nonselectively absorbing or nonabsorbing metal oxides, metal suboxides, metal oxide hydrates as an outer layer, are preferred. Particles described above can be obtained commercially, e.g. as Ronaspheres® or Eusolex®UV-Pearls™ from Merck KGaA, Darmstadt. These pigments are advantageous in cosmetic or pharmaceutical formulations related to their spherical shape. Antimicrobial pigments based on these pigments show, depending on the material, good wrinkle hiding effects and a good skin feeling, and can be used as fillers or in the case of the capsules as well as an active ingredient with combined features such as antimicrobial activity and for example UV-filtering activity. Furthermore, antimicrobial pigments based on these substrates also reduce the gloss of the skin and give to the skin surface a smoother appearance. In addition, the skin feeling is improved, because of the glide and roll effect of the antimicrobial spheres. In oral care applications for example antimicrobial low abrasive spheres can advantageously be used. These particles combine the antimicrobial activity with the low abrasive properties of the spheres.

The mean diameter of the spherical particles or capsules can vary between 5 nm and 100 µm, preferably between 8 nm and 50 µm and most preferably from 8 nm to 5 µm. Spherical metal oxides, in particular metal oxides with UV-filtering activity, preferably have a mean diameter of 5 to 100 nm, especially of 8 to 50 nm and most preferably of 8 to 30 nm. A large surface area characterizes these particles, which therefore can advantageously be used as substrate for antimicrobial pigments according to the present invention. The antimicrobial activity is combined with for example the UV-filtering activity, thus providing multifunctional materials.

In a further embodiment, antimicrobial pigments according to the present invention can additionally be further coated with a protective coating layer. The protective coating layer is believed to influence the rate at which the antimicrobial component diffuses from a dispersed particle into the

application matrix. The small residual porosity of the silica or alumina coating, for example, also allows the antimicrobial component to diffuse through at a slow controlled rate thus extending the duration of the antimicrobial activity. Further, the ability to adjust the dispersibility of the particulate compositions of this invention both increases their use efficiency and improves the quality of the product. The antimicrobial particles may further comprise a tertiary coating layer of a hydrous metal oxide, which is much less agglomerated and disperse readily in polymers. For example, a tertiary coating of hydrous alumina or magnesia will raise the isoelectric point of the composition. The control of the isoelectric point between about 5.5 and about 9.5 is beneficial in facilitating the dispersion and/or flocculation at the particulate compositions during plant processing and in their end use applications. This both increases the use efficiency of the antimicrobial pigments and improves the quality in applications. Enhanced dispersibility also can be impacted by micronizing the product with small levels, e.g. 0.1 to 1 % of organic dispersion aids. Dispersion aids may be incorporated either with the antimicrobial pigments or in the process for incorporating them in applications.

The protective coating is selected from silica, silicates, borosilicates, aluminosilicates, alumina, aluminum phosphate, or mixtures thereof. The protective coating functions as a barrier between the antimicrobial outer layer and an application matrix in which it may be incorporated, minimizing interaction with the application matrix. This protective coating also is believed to influence the rate at which the antimicrobial component diffuses from a dispersed pigment into the application matrix.

The protective protective coating layer corresponds to 0.5 to 20 % by weight based on the antimicrobial pigments, and preferably, e.g., 1 to 5 % by weight of silica or e.g., 1 to 6 % by weight of alumina in the coated antimicrobial pigment. It will be appreciated by those skilled in the art that if fine particles of a substrate are employed in carrying out the invention, the

practitioner should assure total surface coverage of the first coated substrate. The protective layer of silica or alumina can be quite dense although it must be sufficiently porous to permit diffusion of the antimicrobial metal ions through the coating at a slow rate, while  
5 functioning as a barrier which limits interaction between the antimicrobial layer and the application matrix in which it is distributed. Silica is a preferred coating material because of the relative ease with which dense, uniform coatings can be obtained. Silica-coated particles may have a low isoelectric point and may tend to be difficult to disperse in organic  
10 materials. The isoelectric point represents the pH at which a particle surface carries zero electric charge. Control of the isoelectric point between 5.5 and 9.5 is beneficial in facilitating the dispersion and/or flocculation of the particulate compositions during plant processing and in their end use applications. Therefore, for particles coated with silica or related materials  
15 with a low isoelectric point, a tertiary coating of hydrous alumina or magnesia or other metal oxide may be added to raise the isoelectric point. For example, hydrous oxides of Al, Mg, Zr and the rare earths, may bring the isoelectric point into the range of 5.5 to 9.5. Hydrous alumina, typically as a mixture of boehmite ( $\text{AlOOH}$ ) and amorphous alumina ( $\text{Al}_2\text{O}_3\cdot\text{H}_2\text{O}$ ), is a  
20 preferred tertiary coating material. Isoelectric points in a preferred range of 5.5 to 8.8 can readily be obtained with alumina coatings. For higher isoelectric points, magnesia is preferred. Dispersion aids may be incorporated either with the antimicrobial pigments or in the process for incorporating them in applications to facilitate dispersion in end use  
25 applications.

In an alternative embodiment of the invention, alumina may be selected as the protective coating and a further coating may not be needed to adjust the isoelectric point. When alumina is used as the protective coating, the  
30 isoelectric point of the resulting pigment typically will be in the preferred range.

Antimicrobial pigments according to the present invention can be obtained in a simple way. Accordingly, methods for the preparation of antimicrobial pigments are also part of the present invention. A preferred process for the production of the antimicrobial pigments according to the present invention includes the agitation of a suspension comprising one or more inorganic pigments and silver oxide as antimicrobial component. The process is based on a process described by A. Goetz, E. C. Y. Inn in *"Reversible Photolysis of Ag Sorbed on Colloidal Metal Oxides"* in *Rev. Modern Phys.* 1948, 20, 131-142.

The preparation can be performed in water, ethanol, methanol, 1-propanol, 2-propanol and/or mixtures thereof, preferably water is used. The preparation temperature can vary between 10 and 60°C, preferably between 20 and 45°C and is most preferably held at 37°C.

The suspension is agitated from 4 up to 24 hours, preferably from 8 to 20 hours, and most preferably from 10 to 18 hours.

The progress of the reaction can be easily controlled. The initial dark colour of the reaction mixture, which depends on the concentration of silver oxide, turns to colourless at the end of the reaction. Similar pigments with antimicrobial activity can be obtained by substituting silver oxide by other antimicrobial compounds, such as for example silver salts, for example silver halogenide, silver nitrate, silver sulfate, silver carboxylates such as silver acetate, silver benzoate, silver carbonate, silver citrate, silver lactate, silver salicylate, but also copper oxides, copper sulfide, copper nitrate, copper carbonate, copper sulfate, copper halogenides, copper carboxylates, zinc oxide, zinc sulfide, zinc silicate, zinc acetate, zinc chloride, zinc nitrate, zinc sulfate, zinc gluconate, zinc citrate, zinc phosphate, zinc propionate, zinc salicylate, zinc lactate, zinc oxalate, zinc iodate, zinc iodide or combinations thereof. Silver oxide, silver acetate copper sulfate, zinc acetate are the most preferably used.

The amount of the antimicrobial compound is in the range of 0.001 to 10% by weight, preferably 0.005 to 5% by weight and most preferably 0.01 to 0.5% by weight, based on the inorganic pigment.

5

The resulting antimicrobial pigments can be separated using any method known for a person skilled in the art. Preferably the product is filtrated or filtrated with suction and washed with water. Additionally the silver treated pigments can be further washed with organic solvents, such as acetone, to remove residual water. The pigments according to the present invention can be dried. Preferably the antimicrobial pigments are dried in an oven, most preferably at a temperature below 50°C, or by using a vacuum pump or a continuous flash evaporator, most preferably by evaporation of the solvents in vacuum.

15

The production process described can be performed easily and adds an antimicrobial activity to the features of the introduced inorganic pigment, such as colour, transparency, lustre or interference. All compounds needed are readily available and can be easily handled. The process can be performed directly following the production process of the pigments without technical expense.

20

It is believed that pigments according to the present invention are formed via an ion exchange reaction between protons or ions and antimicrobial ions of the antimicrobial compounds, such as for example silver ions, resulting in silver ions bonded to moieties of the inorganic pigment, for example Si-O<sup>-</sup> or Ti-O<sup>-</sup> moieties. These oligodynamically active structures can approximately be described as silver silicates or silver titanates. The source of silver ions for the reaction is for example silver oxide, which is only slightly soluble in water. However, the few silver ions that are at any time present in solution are capable of replacing protons on the surface area of the inorganic pigments forming water as the only reaction product

25

30

besides the antimicrobial pigments. During the course of investigation further analytical experiments revealed the absence of silver metal or silver oxide simply deposited on the surface encouraging silver silicate or silver titanate to be the most relevant structures.

5

In a further embodiment of a method for producing pigments according to the present invention, antimicrobial pigments are further coated with a protective coating layer. Usable materials for the protective coating layer are mentioned above. Any method known for a person skilled in the art can be used to coat the antimicrobial pigments with the protective coating layer, preferably the coating is performed wet-chemically. In the case of a silica coating, active silica is added to the agitated aqueous suspension heated to a temperature between 60 and 90°C, while maintaining the pH of the suspension in the range of 6 to 11. The procedure is described in detail in U.S. Pat. No. 2,885,366, the teachings of which are incorporated herein by reference. Active silica, a low molecular weight form of silica, such as silicic acid or polysilicic acid, may be added to the suspension, or formed in situ as by the continuous reaction of an acid with an alkali silicate. Potassium silicate is generally preferred since the potassium ion has little tendency to coagulate active silica. The bulk commodity is also more stable, which is advantageous from the standpoint of shipping and storing. The silica content of the coated composition is between 0.5 and 20 % by weight and most commonly it is between 1 and 5 % by weight.

25

During the silica deposition it is desirable to maintain substantially uniform conditions in the reaction zone to minimize precipitation of free silica gel. This is preferably accomplished by maintaining good agitation and introducing the reactants in a manner that does not allow local over-concentration. The pH is allowed to fall gradually to about 6 as the process is completed and the slurry is then cured to permit completion of the deposition of silica onto the surface of the antimicrobial pigments. The curing step consists of holding the slurry at temperatures between 60 and

30

90°C, preferably between 75 and 90°C, for from about one-half to two hours, preferably about one hour, while maintaining the pH of the agitated slurry between 6 and 7.5:

5       Alternatively, the antimicrobial pigments may be coated with alumina. This is accomplished by the addition, to the agitated aqueous suspension of the antimicrobial particles heated to between 60 and 90°C, of an alkali aluminate solution or other soluble aluminum salt, e.g., aluminate nitrate while maintaining the pH in the range 6 to 11 by the concurrent addition of  
10       acid or base, as required. Sodium aluminate is preferred, because it is commercially available as a solution, such as Vining's Solution. It is desirable to increase the density of the amorphous alumina phase in the coating by the addition of polyvalent anions selected from the group consisting of sulfate, phosphate and citrate. As in the case of the silica  
15       coating a small residual porosity is necessary to allow the antimicrobial species to diffuse through the protective coating. The alumina content of the coated composition is between 0.5 and 20 % by weight and preferably between 1 and 6 % by weight. The concentration of polyvalent anion in the suspension is about 0.5 % by weight based on the alumina used to coat  
20       the particles.

The product is then recovered as a dry powder, consisting of antimicrobial pigments coated with silica, alumina or silica/alumina, by filtration or centrifugation combined with aqueous washing to remove soluble salts. A  
25       vacuum rotary-type filter is particularly suitable since washing can be carried out without removing the product from the filter.

One major advantage of antimicrobial pigments according to the present invention is combination of different properties of the basis materials with  
30       the antimicrobial activity, for example the combination of colour and antimicrobial activity. Depending on the concentrations of the antimicrobial compound reacted with the basis materials, variations of the colour are also



possible. In the case of high concentrations of the antimicrobial compound differences with respect of the colour can be observed. In some case this is desirable to modify the colour to some extent. Preferably, the colour of the employed inorganic pigment and the antimicrobial pigment does not show a visually noticeable difference. Employed inorganic pigments means all above described pigments, which can be treated with for example silver oxide. One physical parameter for the verification of the latter observation is according to the Hunter model the comparison of the L, a and b values for the employed inorganic pigments and the antimicrobial pigments. The L value is for lightness, the a value is for redness-greenness and the b value is for yellowish-bluish. The a scale has a positive or negative value. Where the a value is positive, the perceived colour is reddish. Where the a value is negative, the perceived colour is greenish. Thus, the more positive the number, the more red the product. The more negative the number, the more greener the product. Similar is true for the b measurement. Where the b value is positive, the perceived colour is yellowish. Where the b value is negative, the perceived colour is bluish. Lightness L is measured on a scale of 0-100 where 0 is black and 100 is white. The L, a and b values of the employed inorganic pigments and the antimicrobial pigments have preferably a maximum deviation for the L value of  $-6 \leq \Delta L \leq 6$ , preferably of  $-5 \leq \Delta L \leq 5$  and most preferably of  $-4 \leq \Delta L \leq 4$ , for the a value of  $-5 \leq \Delta a \leq 5$  and most preferably of  $-3 \leq \Delta a \leq 3$  and for the b value of  $-5 \leq \Delta b \leq 5$ , most preferably of  $-3 \leq \Delta b \leq 3$ .

Antimicrobial pigments according to the present invention can be used for the inhibition of the growth and progeny of microorganisms. Microorganisms in the latter sense are for example bacteria (gram positive and gram-negative bacteria), yeasts, fungi and viruses. Examples of microorganisms described herein are microorganisms selected from for example Staphylococci, Micrococci, Escherichia, Pseudomonas, Bacilli, Salmonella, Shigella, Porphyromonas, Prevotella, Wolinella,

Campylobacter, Propionibacterium, Streptococci, Corynebacterium, Treponema, Fusobacterium, Bifidobacterium, Lactobacillus, Actinomyces, Candida, Malazessia, Aspergillus, herpes simplex 1 and 2.

- 5 The antimicrobial pigments show a good microbicidal activity, that means the number of germs in a medium can be reproducibly decreased. In particular the number of bacteria can be decreased by at least a factor  $10^3$  over a time period of 14 days (starting with an inokulum of  $10^5$ - $10^6$  bacteria/g/ml). In particular, the number of yeasts and fungi can be
- 10 decreased by at least a factor 10 over a time period of 14 days (starting with an inokulum of  $10^5$ - $10^6$  fungi or yeasts/g/ml).

- The antimicrobial activity of the pigments according to the present invention can be shown by tests known for a person skilled in the art, for example
- 15 those based on DIN 58940 and 58944.

- Besides the colour and antimicrobial activity of the pigments they also show depending on the pigment good application behaviour such as dispersibility, a wrinkle-hiding effect, good skin feeling or a good chemical
- 20 stability. These advantageous properties of the used pigments can also predominantly and unaltered be found in antimicrobial pigments according to the present invention, thus providing multifunctional pigments showing colour, good application behaviour, depending on the substrate UV-filtering properties, combined with antimicrobial activity.

- 25 Therefore, in a preferred embodiment of the invention antimicrobial pigments according to the present invention can be used in formulations or applications, such as for example cosmetic formulations, paints, inks, food colouring, home care products, animal care products, products for personal
- 30 and work hygiene, contact lenses, chromatography materials, medical equipment, protective topicals, pharmaceutical, especially dermatological formulations, lacquers, coatings and/or plastics. In more detail formulations

and applications can mean for example antimicrobial cleansers, soaps, disinfectants, anti-fouling and antimicrobial paints for inside and outside use, antimicrobial wallpapers, antimicrobial dressings and plasters, prostheses and bone cement with antimicrobial activity, dental fillings, dental prostheses, formulations against gastrointestinal infections, active coal, antimicrobial cat litter, antimicrobial diapers, tampons or sanitary towels, ambient fragrances for rooms or cars, formulations for oral or body care, absorbent pads, air conditioning (filters and ducts), air inflated construction (air halls), agricultural and mulch films, all purpose adhesives, appliances and equipment, appliance adhesives and sealants, aprons, artificial leather, artificial plants, artificial wood, and plastic lumber, astroturf, automobile parts, automotive and truck upholstery, awnings, bags, bandages, barrier fabrics, bathroom accessories, bathtubs, bedding, beverage dispensers, bibs, boats, boat covers, book covers, bottles, brush bristles, brush handles, brooms, building components (walls, wallboard, floors, concrete, siding, roofing, shingles, hardware, carpet cleaner, ceilings and commercial and industrial applications), cable sheathing, caps (hats), cardboard, carpet and carpet underlay, caster wheels, cat litter, clinical thermometers, coats, compact discs, convertible tops, cookware, coolers, cooling towers, counter and table tops, conveyor belts, countertops, credit cards, crates (food and non-food), cups, currency, curtains, cushion pads, cutting boards, decking, dishes, dish cloths, dishwasher components, diving equipment or snorkels, drainage sewer pipe, draperies, exercise equipment, equipment for slaughterhouses or creameries or dairies, equipment for gyms, saunas or massages, fan blades, fibrefill, filters, fittings, fences, floor coverings, floor and carpet baking, flooring, foam (cushion, mattress), food preparation appliances, food and beverage processing equipment, food and drink containers, storage and bags, food handling equipment, food packaging, food and meat crates, food trays and covers, food wrap, footwear (including boots, sports equipment, and tools), fruit and vegetable brushes, fruit crates, furniture, garbage bags, garbage cans, garment bags, gaskets, general purpose containers, gloves, gowns

(medical and consumers), grease traps, rigid greenhouses, greenhouse films, grout and joint compound, heating, ventilation and air conditioning, hoses, ice-making equipment and trays, incontinence care products, indoor and outdoor furniture, industrial equipment, inflatable bed, insulation for  
5 wire and cable, insulators, intimate apparel, jacket liners, janitorial equipment, kitchen and bathroom hardware, kitchen sinks and fixtures, kitchen towels, laminate and tile adhesives, laying batteries, life vests, liners, mats, mattress cover pads and filling, mattress adhesives, medical and dental apparel, mobile homes, mobile toilets, mops, money, natural  
10 and synthetic fibres and fabrics, non-woven fabrics, outerwear, packaging, pallets, paper products (wipes, tissues, wall coverings, towels, book covers, mulch), pillow covers, pipes, pipe sealant and insulating materials, plaster, plastic films, plates and utensils, playground equipment, plumbing supplies and fixtures (including toilet bowl seats), plumbing adhesives and sealants,  
15 pool liners, process vessels, protective covers, refrigerator components, roofing sheets, membranes, shingles and flashing, ropes, rugs, sales counter, sails, sanitary pipes, sealing compounds for bathrooms, kitchens or glass, sheets and blankets, shoes, shoe insoles, shower curtains, shower tubs, siding for housing, silage wrap, silos, sinks, siphons, skylights,  
20 sleeping bags, sleepwear, socks and hosiery, sponges, sprinkler, sportswear and sports equipment, storage containers, stucco, sun roof, sun shades, napkins, tanks, tape, tarps, telephone boxes or public phones, tents and other outdoor equipment, ticking (mattress pillow), tiles, tile grout, toothbrush handle and bristles, toilet paper and handkerchiefs, toilet blocks  
25 and cleaners, towels, toothbrush tumbler, toys, trim for outerwear and garments, trunk liners, tubing, umbrellas, undergarments, uniforms, upholstery, vacuum cleaner bags, wall and floor covering, wallpaper, waste bags, water tanks, waste containers, water treatment, water and ice handling equipment and filters, wet suits, wipes, wire and cable, wood,  
30 wood filled plastics. Cosmetic formulations can be in the form of solutions, suspensions, emulsions, pasta, ointments, gels, creams, lotions, powders, oils, pencils, deodorant-cremes, gels, lotions, emulsions, deodorant sticks,

Roll-ons, sprays and pump sprays or lacquers, especially nail lacquers. In the case of nail lacquers comprising antimicrobial pigments according to the present invention they can be used as well for cosmetic aspects as well as for the treatment or prevention of nail mycosis. The combination of the colour effect with the antimicrobial activity is therefore advantageous. In all these applications the antimicrobial activity of the pigments according to the present invention can advantageously be used. For example, pigment preparations or mixtures comprising antimicrobial pigments are stable and can be stored over a long period of time, thus facilitating the storage and consumption of these mixtures and preparations for the user. In particular in the case of water-based inks, paints and preparations, the antimicrobial activity is of great importance due to rapid fouling and contamination with bacteria of materials in these application areas. The amount of antimicrobial pigments in all these formulations and applications is not crucial per se and can be adapted in each case to obtain the most effective result. Depending on the formulation or application the content preferably lies in the range of 0.1 to 70% per weight, based on the formulation or application.

In all above-mentioned applications the antimicrobial pigments according to the present invention can advantageously be combined with all known preservatives or antimicrobial agents, such as for example phenoxyethanol, triclosan, 7-ethylbicyclooxazolidine, benzoic acid, bronopol, butylparaben, chlorphenesin, diazolidinyl urea, dichlorobenzyl alcohol, dimethyl oxazolidine, DMDM hydantoin, ethylparaben, hexamidine diisethionate, imidiazolidinyl urea, imidiazolidinyl urea NF, iodopropynyl butylcarbamate, isobutylparaben, methylparaben, potassium sorbate NF FCC, propylparaben, quaternium-15, sodium benzoate NF FCC, sodium caprylate, sodium dehydroacetate, sodium dehydroacetate FCC, sodium hydroxymethylglycinate, sodium hydroxymethylglycinate, sodium methylparaben, sodium propylparaben, sorbic acid NF FCC, anisic acid, benzethonium chloride, caprylic/capric glycerides, caprylyl glycol, di-alpha-

tocopherol, ethylhexylglycerin, glyceryl caprate, methyl isothiazolinone, polymethoxy bicyclic oxazolidine. Tocopheryl acetate, alcohol, benzalkonium chloride, benzethonium chloride, camellia sinensis leaf extract, candida bombicola/glucose/methyl rapeseedate, hydrogen  
5 peroxide, methylbenzethonium chloride phenol, pinus pinaster bark extract, Poloxamer 188, PVP-Iodine, Rosmarinus officinalis Leaf extract, Vitis vinifera seed extract, ammonium benzoate, ammonium propionate, 5-Bromo-5-nitro-1,3-dioxane, Chloroxylenol, Ethyl alcohol, Glutaral, Iodopropynyl butylcarbamate, Isothiazolinone, Parabens, Pircotone  
10 olamine, Selenium disulphide, Sorbic acid (mold), Zinc pyrithione, Benzalkonium chloride, Benzethonium chloride, Benzoic acid, Dehydroacetic acid, Dimethyl hydroxymethyl pyrazole, Formaldehyde, Hexetidine, Methyl dibromo glutaronitrile, Salicylic acid, Sodium hydroxymethylglycinate, Sodium iodate, Zinc oxide, Benzyl alcohol (mould),  
15 Boric acid (yeast), Chloroacetamide, Phenoxyethanol, Orthophenylphenol, Benzalkonium chloride, Benzethonium chloride, 5-Bromo-5-nitro-1,3-dioxane, Bronopol, Diazolidinyl urea, Dimethyl hydroxymethyl pyrazole, Dimethyl oxazolidine, DMDM hydantoin, Ethyl alcohol, 7-Ethyl bicyclooxazolidine, Formaldehyde, Glutaral, Imidazolidinyl urea,  
20 Isothiazolinone, Methenaminium chloride, Methylbromo glutaronitrile, Parabens, Polymethoxy bicyclooxazolidine, Quaternium-15, Sodium hydroxymethylglycinate, Thimersal, Benzoic acid, Benzyl alcohol, Chlorhexidine, Hexetidine, Phenethyl alcohol, Polyaminopropyl biguanide, Polyquaternium-42, Salicylic acid, Sodium iodate, Triclocarban, Triclosan,  
25 Zinc phenolsulphonate, Chloroacetamide, Chlorobutanol, Dehydroacetic acid, Neem seed oil, Parabens, Phenoxyethanol, Tea tree oil, Usnic acid, Ammonium Benzoate, Ammonium Propionate, Benzisothiazolinone, Benzoic Acid, Benzotriazole, Benzyl Alcohol, Benzylhemiformal, Benylparaben, 5-Bromo-5-Nitro-1,3-Dioxane, 2-Bromo-2-Nitropropane-1,3-Diol, Butyl  
30 Benzoate, Butylparaben, Calcium Benzoate, Calcium Paraben, Calcium Propionate, Calcium Salicylate, Calcium Sorbate, Captan, Chloramine T, Chlorhexidine Diacetate, Chlorhexidine Digluconate, Chlorhexidine

Dithydrochloride, Chloroacetamine, Chlorobutanol, p-Chloro-m-Cresol, Chlorophene, p-Chlorophenol, Chlorothymol, Chloroxyleneol, Citrus Grandis (Grapefruit) Fruit Extract, Citrus Grandis (Grapefruit) Seed Extract, Copper Usnate, m-Cresol, o-Cresol, p-Cresol, DEDM Hydantoin, DEDM Hydantoin

5 Dilaurate, Dehydroacetic Acid, Diazolidinyl Urea, Dibromopropamide Diisethionate, Dimethyl Hydroxymethyl Pyrazole, Dimethylol Ethylene Thiourea, Dimethyl Oxazolidine, Dithiomethylbenzamide, DMDM Hydantoin, DMHF, Domiphen Bromide, Ethyl Ferulate, Ethylparaben, Ferulic Acid, Formaldehyde, Glutaral, Glycerol Formal, Glyoxal,

10 Hexamidine, Hexamidine Diparaben, Hexamidine Paraben, 4-Hydroxybenzoic Acid, Hydroxymethyl Dioxazabicyclooctane, Imidazolidinyl Urea, Iodopropynyl Butylcarbamate, Isobutylparaben, Isodecylparaben, Isopropyl Cresols, Isopropylparaben, Isopropyl Sorbate, Magnesium Benzoate, Magnesium Propionate, Magnesium Salicylate, MDM Hydantoin,

15 MEA-Benzoate, MEA o-Phenylphenate, MEA-Salicylate, Methylchloroisthiazolinone, Methylidibromo Glutaronitrile, Methylisothiazolinone, Methylparaben, Mixed Cresols, Nisin, PEG-5 DEDM Hydantoin, PEG-15 DEDM Hydantoin, PEG-5 Hydantoin Oleate, PEG-15 DEDM Hydantoin Stearate, Phenethyl Alcohol, Phenol, Phenoxyethanol,

20 Phenoxyethylparaben, Phenoxyisopropanol, Phenyl Benzoate, Phenyl Mercuric Acetate, Phenyl Mercuric Benzoate, Phenyl Mercuric Borate, Phenyl Mercuric Bromide, Phenyl Mercuric Chloride, Phenylparaben, o-Phenylphenol, Polyaminopropyl Biguanide, Polyaminopropyl Biguanide Stearate, Polymethoxy Bicyclic Oxazolidine, Polyquaternium-42; Potassium

25 Benzoate, Potassium Ethylparaben, Potassium Methylparaben, Potassium Paraben, Potassium Phenoxide, Potassium o-Phenylphenate, Potassium Propionate, Potassium Propylparaben, Potassium Salicylate, Potassium Sorbate, Propionic Acid, Propyl Benzoate, Propylparaben, Quaternium-8, Quaternium-14, Quaternium-15, Silver Borosilicate, Silver Magnesium

30 Aluminium Phosphate, Sodium Benzoate, Sodium Butylparaben, Sodium p-Chloro-m-Cresol, Sodium Dehydroacetate, Sodium Ethylparaben, Sodium Formate, Sodium Hydroxymethane Sulfonate, Sodium

Hydroxymethylglycinate, Sodium Isobutylparaben, Sodium Methylparaben, Sodium Paraben, Sodium Phenolsulfonate, Sodium Phenoxide, Sodium o-Phenylphenate, Sodium Propionate, Sodium Propylparaben, Sodium Pyrithione, Sodium Salicylate, Sodium Sorbate, Sorbic Acid, TEA-Sorbate, 5 Thimerosal, Triclocarban, Triclosan, Undecylenoyl PEG-5 Paraben, Zinc Pyrithione or combinations thereof, such as for example Benzyl alcohol/mehtylchloroisothiazolinone/methylisothiazolinone, Benzyl alcohol/PPG-2 methyl ether/bronopol/deceth-8/iodopropynyl/butylcarbamate, Chloroacetamide sodium benzoate, 10 Dehydroacetic acid/benzyl alcohol, Diazolidinyl urea/iodopropynyl butylcarbamate, Diazolidinyl urea/methylparaben/ethylparaben/butylparaben/propylparaben/isobutylparaben/2-phenoxyethanol, DMDM hydantoin/iodopropynyl butylcarbamate, Glycerin/water/ethoxdiglycol/caprylyl glycol/sodium polyacrylate, Glyceryl 15 laurate/caprylyl/phenylpropanol/dipropylene glycol, Isopropylparaben/isobutylparaben/butylparaben, Methyl chloroisothiazolinone/methyl isothiazolinone, Methyl dibromo glutaronitrile/methylchloroisothiazolinone/methylisothiazolinone/phenoxyethanol, Methyl dibromo glutaronitrile/phenoxyethanol, 20 Methylchloroisothiazolinone/methylisothiazolinone, Methylparaben/ethylparaben/butylparaben/propylparaben/butylenes glycol, Methylparaben/ethylparaben/butylparaben/propylparaben/isobutylparaben, Methylparaben/ethylparaben/butylparaben/propylparaben/isobutylparaben/2-phenoxy-ethanol/bronopol, 25 Methylparaben/ethylparaben/butylparaben/propylparaben/1,3-butylene glycol isomer, Methylparaben/propylparaben, Methylparaben/propylparaben/benzyl alcohol, Methylparaben/propylparaben/bronopol/phenoxyethanol, Methylparaben/propylparaben/bronopol/propylene glycol, 30 Methylparaben/propylparaben/ethylparaben, Methylparaben/propylparaben/propylene glycol/diazolidinyl urea, Phenoxyethanol/benzoic acid/dehydroacetic acid, Phenoxyethanol/benzyl



- alcohol/potassium sorbate/tocopherol,  
Phenoxyethanol/chlorphenesin/glycerin/methylparaben/benzoic acid,  
Phenoxyethanol/DMDMhydantoin/Iodopropynyl butyl carbamate,  
Phenoxyethanol/DMDM hydantoin/methylparaben/propylparaben,  
5 Phenoxyethanol/isopropylparaben/isobutylparaben/butylparaben,  
Phenoxyethanol/methyldibromo glutaronitrile/iodopropynyl butylcarbamate,  
Phenoxyethanol/methylparaben/butylparaben/ethylparaben/propylparaben,  
Phenoxyethanol/methylparaben/butylparaben/ethylparaben/propylparaben/i  
sobutyl-paraben,  
10 Phenoxyethanol/methylparaben/isobutylparaben/butylparaben,  
Phenoxyethanol/triethylene glycol/dichlorobenzyl alcohol, Polyaminopropyl  
biguanide/parabens/phenoxyethanol, PPG-2 methyl ether/sodium  
benzoate/potassium sorbate/iodopropynyl butylcarbamate, Propylene  
glycol/benzyl alcohol/methylchloroisoithiazolinone/methylisothaizolinone,  
15 Propylene glycol/diazolidinyl urea/iodopropynyl butylcarbamate, Propylene  
glycol/diazolidinyl urea/methylparaben/propylparaben, Propylene  
glycol/MDMD hydantoin/methylparaben, Propylene glycol/MDMD  
hydantoin/methylparaben/propylparaben, Propylene glycol/lichen extract,  
Propylene glycol/phenoxyethanol/chlorphenesin/methylparaben, Sodium  
20 levulinate/phenylpropanol combinations. The combination of antimicrobial  
pigments according to the present invention with preservatives or  
antimicrobial agents shown above helps to decrease the amount of the  
preservative or antimicrobial agent in formulations or applications, which is  
advantageous with respect to the regulatory status and the compatibility  
25 with the skin, especially in topical applications.

Furthermore, antimicrobial pigments according to the present invention can  
be advantageously combined with antibiotics. Antibiotics in this sense  
mean all known antibiotics, for example selected from the group of Beta-  
30 lactam, Vancomycin, Macrolides, Tetracyclines, Quinolones,  
Fluoroquinolones, Nitrated compounds (as for instance Nitroxoline,  
Tilboquinol or Nitrofurantoin), Aminoglycosides, Phenicols, Lincosamids,

Synergistins, Fosfomycin, Fusidic acid, oxazolidinones, Rifamycins, Polymixynes, Gramicidins, Tyrocydine, Glycopeptides, Sulfonamides or Trimethoprim. Combinations of antimicrobial pigments and antibiotics are advantageous with respect to the resistance of several microorganisms against certain antibiotics. A combination of antibiotics with antimicrobial pigments according to the present invention helps to overcome the resistance by simply decreasing the number of microorganisms, which have not been affected by the antibiotics.

In several application areas the antimicrobial activity can be useful in several stages of the processing. For example plastics or polymers comprising antimicrobial pigments according to the present invention can be stored in the form of Masterbatches for a long period of time, without risking the contamination of the Masterbatch with microorganisms. The Masterbatch can be processed in the same way as all known Masterbatches. The therewith-obtained products are useful in building and construction, household, items and furnishing, electrical and electronics parts, apparel, textiles and fabrics, coatings and laminates, transportation and recreation, adhesives, sealants and grouts, food contact items and water contact items, such as for example plastic bottles, bottle caps, films, coextrusion films, exterior and interior automotive parts etc, having surfaces, which again show antimicrobial activity. In particular bottles and films comprising pigments according to the present invention are of interest with respect to the decrease of the number of microorganisms in therein-packaged products and consumer goods. Also plastics or polymers used in baths, swimming pools, kitchens, joints compounds, sealing compounds or other in general in humid surroundings can advantageously be pigmented with pigments according to the present invention thus combining colour impression and antimicrobial activity. Suitable plastics and polymers from which the articles are fabricated include synthetic, natural and semisynthetic organic polymers. Example of polymers that can be used to practice this invention include, but are not limited to, aliphatic and aromatic

polyesters, including polyethylene terephthalate, polybutylene terephthalate, polyethylene isophthalate, polyhexamethylene terephthalate, polylactic acid, polyglycolic acid; and liquid crystalline polymers for high performance resins and fibers; polyester block copolymers; aliphatic and aromatic polyamides including nylon 6, nylon 66, nylon 610, nylon 11, nylon 12, nylon 1212, poly-p-phenylene terephthalamide, poly-m-phenylene isophthalamide; copolymerised polyamides; polyolefins including polyethylene, polypropylene, and copolymers thereof; vinyl polymers, including polystyrene, polyacrylonitrile, polyvinylalcohol, polyvinyl acetate, polyvinylchloride, polyvinylidene chloride, ABS resins and acrylic resins; copolymers of ethylene and vinyl acetate; fluorocarbon polymers, including polytetrafluoroethylene, polyvinylidene fluoride and polyvinyl fluoride; polyurethanes; segmented polyurethane elastomers, spandex or elastane elastomers; polyethers, including polyacetals; polyketones, polyetherether ketone (PEEK), polyether ketoneketone (PEKK); polyether and polyester block polymers; polysulfides; polysulfones; polysiloxanes such as polydimethyl siloxane; polycarbonates; thermosetting synthetic polymers such as phenol-formaldehyde copolymer, polyurethane, polyesterurethane, polyetherurethane, polyetherurethaneurea, polyesterurethaneurea; natural polymers such as cellulose, cotton and wool; and regenerated or semi-synthetic polymers such as rayon, cuprammonium rayon, acetate rayon, triacetate rayon, reconstituted silk and polysaccharides. This group includes reasonable copolymers, terpolymers and blends of many of the species listed. Spandex is defined herein to refer to a fiber or filament made from a long chain synthetic polymer that comprises at least 85 % by weight of segmented polyurethane.

The polymer articles of this invention can be, for example, in the shape of films, fibers, powders, granules or articles made there from such as containers, pipes and monofilaments for brushes. When a high degree of antimicrobial effect is desired, the molded article preferably has a large surface area.

A polymer article of the present invention having antimicrobial properties is comprised of at least one of the aforementioned antimicrobial pigments and at least one organic polymer. The antimicrobial composition accounts  
5 for 0.1 to 60 % by weight, preferably 0.1 to 15 % by weight of the polymer article, and most preferably 0.3 to 2 % weight of the polymer article.

If the antimicrobial composition is incorporated in an amount less than about 0.1 % by weight, the polymer article has insufficient antimicrobial  
10 activity for any useful applications. However, it will be appreciated by those skilled in the art that if extremely fine particles are incorporated into the polymer matrix, then less than about 0.1 % may be acceptable. Above about 60 % by weight there is no significant increase in the antimicrobial activity of the polymer article and the physical properties of the polymer  
15 article start to show some deterioration. This limits the usefulness of the article. Furthermore, the incorporation of high levels of the antimicrobial composition is undesirable from an economic standpoint and because of undesirable effects on the properties of the composite. A preferred upper level for the antimicrobial component is about 15 % weight below which  
20 level there is an optimum combination of antimicrobial activity, polymer article properties and cost efficiency.

When a polymer article according to the present invention has a relatively large thickness, such as containers, pipes, granules or coarse fibers, the  
25 particle size of the antimicrobial pigments may be in the range of a few microns to tens of microns or even up to a hundred microns. When fibers or films are molded as an article according to the present invention, preference is given to a smaller size particle, for instance, a particle size of 5 microns down to a one hundredth of a micron (ten nanometers),  
30 especially less than 2 microns, is commonly employed for fibers intended for use in clothing.

The polymer articles according to the present invention may contain other additives as well as antimicrobial compositions. They may contain, for example, polymerization catalysts, stabilizers, delustering agents, optical whitening agents, organic or inorganic pigments, inorganic fillers, plasticizers and so on. It is also possible that the antimicrobial pigments themselves can fulfill a dual role and provide the benefits of some of the aforementioned additives. Examples of plastics which can be used here as well as preparation and processing methods can be found in RD 472005 or R. Glausch, M. Kieser, R. Maisch, G. Pfaff, J. Weitzel, *Perlglanzpigmente*, Curt R. Vincentz Verlag, 1996, 83 ff.

Paints and lacquers comprising pigments according to the present invention can be waterborne or solvent-based. They can be on the basis of synthetic or chemically modified natural polymers, such as for example, acryl polymers, vinyl polymers, alkyd resins, phenol resins, urea resins, melamine resins, polyester resins, cellulose nitrate, epoxy resins, polyurethane resins, bitumen, tar, shellac, natural rubber or resins, and can comprise all known additives and adjuvants, such as for example sikkatives, waxes, dispersing agents, anti-blocking agents or drying agents. Paints and lacquers pigmented with antimicrobial pigments can be used for example in the automotive area or in the industrial area, in powder coatings, architectural use, as coating of wood, steel, inner walls, floors, blankets, facades or in humid surroundings thus providing the surfaces antimicrobial activity and colour impressions depending on the used pigment. Furthermore the coating is stabilized against attacks of microorganisms thus enhancing the durability of the coatings.

Antimicrobial pigments according to the present invention can advantageously be applied to all kinds of printing inks, such as liquid inks, UV curable inks, paste inks and paper coatings. Known preparations for these application areas lack sufficient stability against antimicrobial contamination, especially in water based systems. The usage of

antimicrobial pigments according to the present invention can help to minimize the contamination with microorganisms thus allowing to decrease the necessary content of preservatives. The therewith pigmented preparations are stable for a long period of time. The liquid inks can be water based, based on water/alcohol mixtures or solvent based. Suitable binders for aqueous inks are acrylates, methacrylates, polyesters and polyurethanes. Binders for solvent based inks are nitrocellulose, ethylcellulose, polyamide, PVC/PVA-copolymers, polyvinylbutyral, chlorinated rubber, rosin modified phenolic resins, maleinic resins, calcium/zinc-resinate-EHEC, acrylates and mixtures thereof. Solvents which can be used in solvent based inks are ethanol, isopropanol, n-propanol, acetone, ethylacetate, isopropylacetate, n-propylacetate, methoxypropanol, ethoxypropanol, toluene, aliphatic hydrocarbons and mixtures. UV-curable printing inks are basically composed of a binder and a liquid monomer, such as epoxy acrylates, polyurethane acrylates, polyester acrylates as reactive monomers hexanediol diacrylate, di/tripropylene glycol diacrylate, trimethylpropane triacrylate, trimethylolpropane ethoxy triacrylate and mixtures thereof. Paste inks containing antimicrobial pigments can further contain rosin modified phenolic resins, maleinic acid modified resins, alkyd resins, linseed/soybean oil based resins, hydrocarbon based resins and mineral oils, linseed oil or soybean oil as solvents. Paper coatings containing antimicrobial pigments may further contain starch, protein/casein, polyvinyl alcohol, latexes, carboxymethyl cellulose or acrylate binders. The printing inks may further contain known fillers and rheology modifiers. More information on technology and compositions of printing inks is provided by R. L. Leach, R. J. Pierce, in The Printing Ink Manual, Fifth Edition, Blueprint, London, 1993.

Optically variable antimicrobial pigments can preferably be combined in inks and paper coatings with any conventional colorant, metal flake pigments and other kinds of effect pigment. Preferably, optically variable

antimicrobial pigments are printed onto a dark background or in combination with dark, but transparent or translucent colorants.

5      Optically variable antimicrobial pigments can be compounded with solvents, surfactants or binders into pigment preparations with improved handling and application properties such as pigment pastes or pearlets, as described by Ullmann, 46th Annual Technical Conference, Oct. 2-4, 2002, National Printing Ink Research Institute, Marco Island, Florida, USA.

10     Various printing techniques are feasible with antimicrobial pigments according to the present invention, such as gravure printing using solvent based liquid inks, flexographic printing using solvent based liquid inks, water based inks or UV-curable inks, offset overprint varnishing with water based or UV-curable inks, screen printing using solvent based screen  
15     printing inks, UV-screen printing processes or water based screen printing, offset printing, including sheet fed offset, web offset, UV offset and waterless offset printing.

20     Furthermore, antimicrobial pigments according to the present invention can be used for prophylaxis and/or treatment of acne, caused by microorganisms, such as *Propionibacterium acnes*, *Propionibacterium granulosum* or *Staphylococcus epidermidis*. *Propionibacterium acnes* are a normal inhabitant of the skin. It uses sebum as a nutrient for growth, therefore increases in follicles during puberty. People with acne have more  
25     *Propionibacterium acnes* in their follicles than people without acne. The presence of bacteria attracts white blood cells to the follicle. These white blood cells produce an enzyme that damages the wall of the follicle, allowing the contents of the follicle to enter the dermis. This process causes an inflammatory response seen as red bumps, pustules and  
30     nodules. The bacteria also cause the formation of free fatty acids, which are irritants, increasing the inflammatory process in the follicle. Suitable formulations comprising antimicrobial pigments according to the present

invention are in the form of soaps, cleansers, solutions, suspensions, emulsions, pasta, ointments, gels, creams, lotions, powders, oils, pencils, sprays. Further ingredients that can be incorporated into the formulations are described later in this application in more detail.

5

Furthermore, deodorants can be pigmented with antimicrobial pigments according to the present invention. Different forms of deodorants are in mind: deodorant-cremes, gels, lotions, emulsions, deodorant sticks, Roll-ons, sprays and pump sprays. The pigments are combined with a suitable carrier material used in deodorants. Examples of suitable carrier materials are glyceryl stearate, aluminium chlorohydrate, propylene glycol, carbomer, glycerin, dicapryl ether, ethanol, glyceryl cocoate, cyclomethicone, dimethicone, dipropylene glycol, stearyl alcohol, mineral oil, phenyltrimethicone or sodium stearate. The odour production of the skin is the result from the modifications of initially odourless secretions from the apocrine glands, such as for example lipids, proteins, ammonia, steroids and reducing sugars, by microorganisms, like for example *Staphylococcus*, *Corynebacterium* or *malassezia*. The antimicrobial pigments are effective against the Gram-positive cocci group, for example against the *Micrococcaceae* family (*Staphylococcus aureus*, *staphylococcus epidermidis*, *staphylococcus hominis*), against the Gram-positive rods, for example against the *Coryneforms* family (*Brevibacterium* and /or *corynebacterium* for example) causing malodour of the skin, which can be reduced by deodorants comprising these pigments. The deodorants may comprise various adjuvants used in this type of composition, such as scents or perfumes, preservatives, electrolytes, silicone derivatives, dyes and/or pigments which colour the composition itself, or other ingredients customarily used for deodorants. Further ingredients that can be incorporated into the formulations are described later in this application in more detail.

30



Antimicrobial pigments according to the present invention can also be used for oral care, for example for prophylaxis and/or treatment of dental plaque, caries or oral malodour. Oral malodour, caries and dental plaque are caused by microorganisms, for example by *Streptococcus sobrinus*,  
5 *Streptococcus mutans*, *Streptococcus gordonii*, *Streptococcus salivaris*, *Streptococcus sanguis*, *Actinomyces*, *Lactobacilli*, *Fusobacterium*, *Veillonella*, *Treponema. denticola*, *Porphyromonas. gingivalis*, *Bacteroides* or *Peptostreptococcus*.

10 The oral composition may be formulated for use in any form of interdental or periodontal treatment and may be in the form, for example, of a dentifrice, mouthwash, toothpowder, chewing gum, lozenge, mouth spray, floss, dental paint, or glass ionomer cement. Use of the antimicrobial material of the present invention in a glass ionomer cement has the  
15 advantage of providing X-ray opacity as well as antimicrobial action.

Such compositions may, as appropriate, contain conventional materials such as, for example, humectants, surfactants, gelling agents, abrasives or low abrasive spheres, fluoride sources, desensitizing agents, flavorings,  
20 colorings, sweeteners, preservatives, structuring agents, bactericides, anti-tartar agents and anti-plaque agents.

Suitable humectants for use in dentifrice compositions include polyhydric alcohols such as xylitol, sorbitol, glycerol, propylene glycol and poly-  
25 ethylene glycols. Mixtures of glycerol and sorbitol are particularly effective. A humectant helps to prevent dentifrice compositions from hardening on exposure to air, and may also provide a moist feel, smooth texture, flowability, and a desirable sweetness in the mouth. Suitably, such humectants may comprise from about 0-85 %, preferably from about  
30 0-60 % by weight of the oral hygiene composition.

5 Suitable surfactants for use in dentifrices, mouthwashes etc. are usually water-soluble organic compounds, and may be anionic, nonionic, cationic or amphoteric species. The surfactant used should preferably be reasonably stable, able to form suds throughout a wide pH range, and able to produce a foam in use.

10 Anionic surfactants include the water-soluble salts of C<sub>10-18</sub> alkyl sulphates (e. g. sodium lauryl sulfates), water soluble salts of C<sub>10-18</sub> ethoxylated alkyl sulphates, water soluble salts of C<sub>10-18</sub> alkyl sarcosinates, the water-soluble salts of sulfonated monoglycerides of C<sub>10-18</sub> fatty acids (e. g. sodium coconut monoglyceride sulfonates), alkyl aryl sulfonates (e. g. sodium dodecyl benzene sulfonate) and sodium salts of the coconut fatty acid amide of N-methyltaurine.

15 Nonionic surfactants suitable for use in oral compositions include the products of the condensation of alkylene oxide groups with aliphatic 'or alkylaromatic species, and may be for example, polyethylene oxide condensates of alkyl phenols, ethylene oxide/propylene oxide copolymers (available from BASF Wyandotte Chemical Corporation under the trade name 'Pluronic'), ethylene oxide/ethylene diamine copolymers, ethylene  
20 oxide condensates of aliphatic alcohols, long chain tertiary amine oxides, long chain tertiary phosphine oxides, long chain dialkyl sulfoxides and mixtures thereof. Alternatives include ethoxylated sorbitan esters such as those available from ICI under the trade name "Tween".

25 Cationic surfactants are generally quaternary ammonium compounds having one C<sub>8-18</sub> alkyl chain and include, for example, lauryl trimethylammonium chloride, cetyl trimethylammonium bromide, cetyl pyridinium chloride, di-isobutylphenoxyethoxyethyl dimethylbenzylammonium chloride, 30 coconutalkyltrimethylammonium nitrite and cetyl pyridinium fluoride. Also useful are benzyl ammonium chloride, benzyl dimethyl stearyl ammonium

chloride, and tertiary amines having one C<sub>1-18</sub> hydrocarbon group and two (poly)oxyethylene groups.

5 Amphoteric surfactants are generally aliphatic secondary and tertiary amines comprising aliphatic species that may be branched or unbranched, and in which one of the aliphatic species is a C<sub>8-18</sub> species and the other contains an anionic hydrophilic group, for example, sulfonate, carboxylate, sulfate, phosphonate or phosphate. Examples of quaternary ammonium compounds are the quaternized imidazole derivatives available under the trade name 'Miranol' from the Miranol Chemical Company.

Suitably, the surfactant is included in an amount of from 0-20 %, preferably 0-10 % by weight of the oral hygiene composition.

15 Structuring agents may be required in, for example, dentifrices and gums to provide desirable textural properties and "mouthfeel". Suitable agents include natural gum binders such as gum tragacanth, xanthan gum, gum karaya and gum arabic, seaweed derivatives such as Irish moss and alginates, smectite clays such as bentonite or hectorite, carboxyvinyl polymers and watersoluble cellulose derivatives such as hydroxyethyl cellulose and sodium carboxymethyl cellulose. Improved texture may also be achieved, for example, by including colloidal magnesium aluminium silicate. Suitably, the structuring agent is included in an amount of from 0-5 %, preferably 0-3 % by weight of the oral hygiene composition.

25 Abrasives should preferably be capable of cleaning and/or polishing the teeth without causing harm to dental enamel or dentine. They are used most commonly in dentifrices and toothpowders, but may also be used in mouthwashes etc. Suitable abrasives include the silica abrasives, such as hydrated silicas and silica gels, particularly silica xerogels such as those available under the trade name 'Syloid' from W. R. Grace and Company. Also suitable are precipitated silica materials such as those available under

30

the trade name 'Zeodent' from J. M. Huber Corporation, and diatomaceous earths such as those available under the trade name 'Celite' from Johns-Manville Corporation. Alternative abrasives include alumina, insoluble metaphosphates such as insoluble sodium metaphosphate, calcium carbonate, dicalcium phosphate (in dihydrate and anhydrous forms), calcium pyrophosphate (including  $\beta$ -phase calcium) polymethoxylates and particulate thermosetting polymerised resins such as, for example, melamine-ureas, melamine-formaldehydes, urea-formaldehydes, melamine-urea-formaldehydes, cross-linked epoxides, melamines, phenolics, highly purified celluloses such as those available under the trade name 'Elcema' from Degussa AG, and cross-linked polyesters. Suitably, abrasives are included in an amount of from 0-80 %, preferably 0-60 % by weight of the oral hygiene composition. As well as abrasives also low abrasive spheres can be added.

Fluoride sources suitable for use in all oral hygiene compositions of the present invention include sodium fluoride, zinc fluoride, potassium fluoride, aluminium fluoride, lithium fluoride, sodium monofluorophosphate, acidulated phosphate fluoride, stannous fluoride, ammonium fluoride, ammonium bifluoride and amine fluoride.

Preferably, the fluoride source is present in an amount sufficient to provide from about 50 ppm to about 4,000 ppm fluoride ions in use. Inclusion of a fluoride source is beneficial, since fluoride ions are known to become incorporated into the hydroxyapatite of tooth enamel, thereby increasing the resistance of the enamel to decay. Fluoride is also now thought to act locally on the tooth enamel, altering the remineralisation-demineralisation balance in favor of remineralisation. Inclusion of a fluoride source is also desirable when a polyphosphate anti-calculus agent is included, in order to inhibit the enzymic hydrolysis of such polyphosphates by salivary phosphatase enzymes.

Suitable desensitizing agents include, for example, formaldehyde, potassium nitrate, tripotassium citrate, potassium chloride and strontium chloride (suitably as hexahydrate), strontium acetate (suitably as hemihydrate) and sodium citrate/Pluronic gel.

Flavoring agents may be added to increase palatability and may include, for example, oils of peppermint, spearmint, wintergreen, sassafras and clove. Sweetening agents may also be used, and these include D-tryptophan, saccharin, dextrose, aspartame, levulose, acesulfam, dihydrochalcones and sodium cyclamate. Typically, such flavoring agents are included in amounts of from 0-5 %, preferably from 0-2 % by weight of the oral hygiene composition. Coloring agents and pigments may be added to improve the visual appeal of the composition. Suitable colorants include dyes, such as FD & C blue No. 1, D & C yellow No. 10 and D & C yellow No. 3. A suitable and commonly used pigment is pigment grade titanium dioxide, which provides a strong white color.

Suitably, as described above, the compositions of the invention may include a further antimicrobial agent as a preservative and/or anti-plaque agent in combination with antimicrobial pigments according to the present invention. Suitable antimicrobial agents include zinc salts (such as zinc citrate), cetyl pyridinium chloride, the bis-biguanides (such as chlorhexidine), aliphatic amines, bromochlorophene, hexachlorophene, salicylanilides, quaternary ammonium compounds and triclosan. Enzymic systems providing a source of a natural biocide may be used as alternatives to or in combination with the biocides listed. For example, a system comprising lactoperoxidase and glucose oxidase may be used to generate antimicrobial amounts of hydrogen peroxide in the presence of glucose, water and oxygen.

The composition may also comprise an anti-calculus agent. Suitable anti-calculus agents include zinc salts such as zinc citrate and zinc chloride and polyphosphates. Suitable pyrophosphates include the sodium and potassium pyrophosphates, preferably disodium pyrophosphate, dipotassium pyrophosphate, tetrasodium pyrophosphate and tetrapotassium pyrophosphate. A preferred source of pyrophosphate is a mixture of tetrasodium pyrophosphate and tetrapotassium pyrophosphate. Suitably, the ratio of tetrasodium pyrophosphate to tetrapotassium pyrophosphate is 0:1 to 3:1, preferably 0:1 to 1:1. Preferably, tetrapotassium pyrophosphate is the predominant species.

The composition may also comprise alcohol. This component is particularly useful in mouthwash formulations, where it may be used to solubilise components that have low solubility in water.

Particularly suitable oral compositions are those in the form of a mouthwash or toothpaste.

Antimicrobial pigments according to the present invention can also be used for prophylaxis and/or treatment of dandruff. Dandruff is a scalp disorder that is characterized by the formation of white or grey scales, accompanied by mild itching. The scales present diffusely and in patches. Dandruff occurs most frequently and most severely in young males, is rare in children and the elderly, and is otherwise common throughout the world's adult population. Dandruff has traditionally been linked to seborrhoea, an inflammatory skin disorder that is known for producing greasy scales superimposed upon reddened skin areas. However, seborrhoea can occur without dandruff, and dandruff can develop in the absence of apparent seborrhoea. Current knowledge suggests that the term "dandruff" is best used to describe the symptom complex of scalp flaking and itching, rather than as a synonym for seborrhoea, which is a specific disease entity. Although dandruff is a possible symptom of seborrhoea, it also can

potentially result from scalp irritation caused by excessive sun exposure, airborne environmental substances, and cosmetic hair products. Dandruff reflects a fundamental abnormality in the dead outer layer of skin ("the scalp") that covers the hairy top of the head. The involved skin cells lack the ability to properly adhere to one another. Consequently, clumps of cells separate from the scalp surface as scales. The shedding of these scales produces flakes of dandruff. A relationship between dandruff and a class of yeast called *malassezia furfur* and *malassezia globosa* has long been recognized. Bacteria and yeast are ordinary occupants of the human scalp. However, in those individuals with dandruff, yeast is present in significantly greater numbers than would normally be expected. Many doctors and researchers believe that inflammation caused by an immune response to the yeast produces the dandruff condition. In this case, a suitable formulation is in the form of a shampoo or lotion for rinsing out, the formulation in question being applied before or after shampooing, before or after colouring or bleaching or before or after permanent waving. It is also possible to choose a formulation in the form of a lotion or gel for styling or treating the hair, in the form of a lotion or gel for brushing or blow-waving, in the form of a hair lacquer, permanent waving composition, colorant or bleach for the hair. The cosmetic formulation may comprise various adjuvants used in this type of composition, such as surface-active agents, thickeners, polymers, softeners, preservatives, foam stabilizers, electrolytes, organic solvents, silicone derivatives, antigrease agents, dyes and/or pigments which colour the composition itself or the hair, or other ingredients customarily used for hair care. Further ingredients that can be incorporated into the formulations are described later in this application in more detail.

Furthermore, antimicrobial pigments according to the present invention can also be used for prophylaxis and/or treatment of herpes, for example herpes labialis or herpes genitalis. The quiet pandemic herpes simplex virus (HSV) infection cannot be cured, that means after primary or initial

infection the virus persists for life in a latent form, periodically reactivating and often resulting in significant psychosocial distress for the patient. The most relevant subtypes of the Herpesviridae with a high incidence rate are HSV-1 and HSV-2. The viruses are the cause of mucocutaneous infections such as oral-facial infections (e.g. herpes labialis, pharyngitis herpetica or herpetic gingivostomatitis predominantly caused by HSV-1), cutaneous infections (e.g. herpetic whitlow and herpes gladiatorum), herpes genitalis or perianal herpes (in the majority of the cases caused by HSV-2). Several in vitro studies have shown that especially silver ions are effective against HSV (e.g. F. Shimizu, Y. Shimizu, K. Kumagai, Antimicrob. Agents-Chemother. 1976, 57-63). Therefore antimicrobial pigments according to the present invention can be used for the treatment of herpes. The treatment can preferably be achieved by topical administration of formulations comprising pigments according to the present invention. The formulations can be for example in the form of creams, solutions, ointments, gels, balms or sticks. For the treatment of infections of the lips, creams, gels, balms, ointments or sticks are especially preferred. In all these formulations the antimicrobial pigments according to the present invention can advantageously be combined with all known substances suitable for the treatment of herpes infections, such as for example acyclovir, valacyclovir, famciclovir, peniciclovir, idoxuridine, vidarabine, trifluridine, foscarnet, ribonucleotide reductase inhibitors, protease inhibitors, docosanol, tin bifluoride, zinc oxide or benzocaine. The amount of the antimicrobial pigments according to the present invention can vary between 0.5 to 20 %, based on the formulation, in particular between 1 to 10 %. Further ingredients that can be incorporated into the formulations are described later in this application in more detail.

The present invention is also directed to formulations or applications comprising antimicrobial pigments according to the present invention. Preferably the formulation or application may furthermore comprise at least one compound selected from the group consisting of suitable substrates for

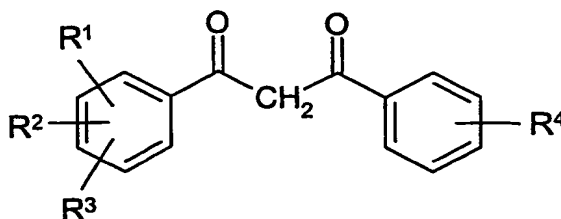


microorganisms, such as for example organic compounds. The suitable substrates for microorganisms are for example selected from the group consisting of alkanes, alkenes, alkynes, with or without functional groups, sugars, polyols, alcohols, saturated or unsaturated carboxylic acids, proteins, amino acids, water, fatty acids, waxes, fats, mineral oils, salts, hormones, steroids, vitamins and/or derivatives or salts thereof. The combination of antimicrobial pigments of the present invention with these substrates allows the broadening of the application area of these substrates, for example in cosmetic formulations. The contamination of formulations containing these substrates is no longer an obstacle for their use. Generally the use of antimicrobial pigments according to the present invention in formulations allows the reduction of the amount or number of preservatives, which have to be added further to the formulation. In particular, there is no need for adding any further preservatives to the formulation.

Formulations or preparations containing pigments according to the present invention usually comprise several ingredients. In the following examples of commonly used ingredients, especially for cosmetic formulations, are given.

Preferred formulations or applications additionally comprise at least one UV filter resulting in antimicrobial preparations having light protection properties. The UV filter can preferably be selected from the group of dibenzoylmethane derivatives. The dibenzoylmethane derivatives used within the scope of the present invention are products which are already well known per se and are described, in particular, in the specifications FR-A-2 326 405, FR-A-2 440 933 and EP-A-0 114 607.

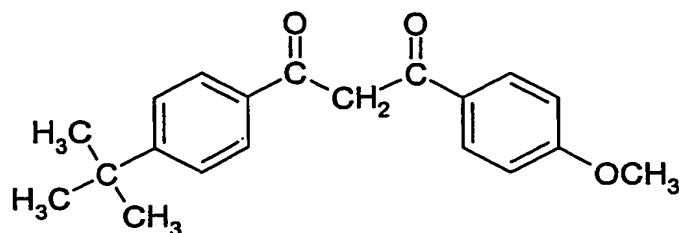
The dibenzoylmethane derivatives which can be used in accordance with the invention may be selected, in particular, from the dibenzoylmethane derivatives of the following formula:



in which  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$  and  $\text{R}^4$ , which are identical to or different from one another, are hydrogen, a straight-chain or branched  $\text{C}_{1-8}$ -alkyl group or a straight-chain or branched  $\text{C}_{1-8}$ -alkoxy group. In accordance with the present invention, it is of course possible to use one dibenzoylmethane derivative or a plurality of dibenzoylmethane derivatives. Of the dibenzoylmethane derivatives to which the present invention more specifically relates, mention may be made, in particular, of:

2-methyldibenzoylmethane, 4-methyldibenzoylmethane, 4-isopropyldibenzoylmethane, 4-tert-butyldibenzoylmethane, 2,4-dimethyldibenzoylmethane, 2,5-dimethyldibenzoylmethane, 4,4'-diisopropyldibenzoylmethane, 4,4'-methoxy-tert-butyldibenzoylmethane, 2-methyl-5-isopropyl-4'-methoxydibenzoylmethane, 2-methyl-5-tert-butyl-4'-methoxydibenzoylmethane, 2,4-dimethyl-4'-methoxydibenzoylmethane and 2,6-dimethyl-4-tert-butyl-4'-methoxydibenzoylmethane, this list being non-restrictive.

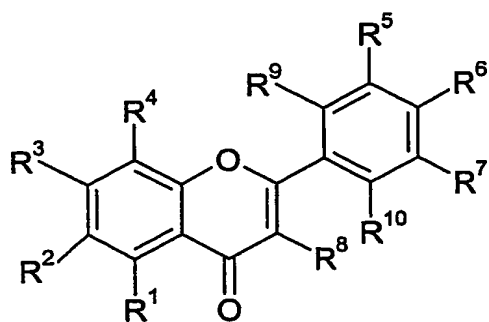
Of the above-mentioned dibenzoylmethane derivatives, particular preference is given in accordance with the invention to 4,4'-methoxy-tert-butyldibenzoylmethane and especially 4,4'-methoxy-tert-butyldibenzoylmethane, which is commercially available under the trade name Eusolex<sup>®</sup> 9020 from Merck KGaA, where this filter conforms to the following structural formula:



5

A further dibenzoylmethane derivative which is preferred in accordance with the invention is 4-isopropylidibenzoylmethane.

10 Additionally, in likewise preferred embodiments of the invention, the preparations according to the invention may also contain compounds of the formula I which have a UV absorption in the UV-A and/or UV-B region:



15

20

where  $R^1$  to  $R^{10}$  may be identical or different and are selected from

- H
- $OR^{11}$
- straight-chain or branched  $C_1$ - to  $C_{20}$ -alkyl groups,
- straight-chain or branched  $C_3$ - to  $C_{20}$ -alkenyl groups,
- straight-chain or branched  $C_1$ - to  $C_{20}$ -hydroxyalkyl groups, where the hydroxyl group may be bonded to a primary or secondary carbon atom of the chain and furthermore the alkyl chain may also be interrupted by oxygen, and/or

30

- C<sub>3</sub>- to C<sub>10</sub>-cycloalkyl groups and/or C<sub>3</sub>- to C<sub>12</sub>-cycloalkenyl groups, where the rings may each also be bridged by -(CH<sub>2</sub>)<sub>n</sub>- groups, where n = 1 to 3,
- where all OR<sup>11</sup> are, independently of one another,
  - 5           - OH
  - straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-alkoxy groups,
  - straight-chain or branched C<sub>3</sub>- to C<sub>20</sub>-alkenyloxy groups,
  - straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-hydroxyalkoxy groups, where the hydroxyl group(s) may be bonded to a primary or secondary carbon atom of the chain and furthermore the alkyl chain may also be interrupted by oxygen, and/or
  - 10           - C<sub>3</sub>- to C<sub>10</sub>-cycloalkoxy groups and/or C<sub>3</sub>- to C<sub>12</sub>-cycloalkenyloxy groups, where the rings may each also be bridged by -(CH<sub>2</sub>)<sub>n</sub>- groups, where n = 1 to 3, and/or
  - 15           - mono- and/or oligoglycosyl radicals,with the proviso that at least 3 radicals from R<sup>1</sup> to R<sup>7</sup> are OH and that at least 2 pairs of adjacent -OH groups are present in the molecule,
- 20   or R<sup>2</sup>, R<sup>5</sup> and R<sup>6</sup> are OH and the radicals R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>7-10</sup> are H.

The flavonoids of the formula I to be employed in accordance with the invention include broad-band UV filters, which can be employed alone or in combination with further UV filters. Other, likewise preferred compounds of the formula I exhibit an absorption maximum in the transition region between UV-B and UV-A radiation. As UV-A-II filters, they therefore advantageously supplement the absorption spectrum of commercially available UV-B and UV-A-I filters. They are insoluble or have low solubility in the preparation matrix. In this case, the compounds are preferably dispersed in the cosmetic preparation in finely divided form. In addition, preferred compounds of this type have advantages on incorporation into the preparations:

- mono- and/or oligoglycosyl radicals improve the water solubility of the compounds to be employed in accordance with the invention;
  - straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-alkoxy groups, in particular long-chain alkoxy functions, such as ethylhexyloxy groups, increase the oil solubility of the compounds;
- 5 i.e. the hydrophilicity or lipophilicity of the compounds according to the invention can be controlled via a suitable choice of substituents.

10 Preferred mono- or oligosaccharide radicals are hexosyl radicals, in particular ramnosyl radicals and glucosyl radicals. However, other hexosyl radicals, for example allosyl, altrosyl, galactosyl, gulosyl, idosyl, mannosyl and talosyl, may also advantageously be used. It may also be advantageous to use pentosyl radicals. The glycosyl radicals may be linked to the basic structure by means of an  $\alpha$ - or  $\beta$ -glycosidic link. A preferred disac-

15 charide is, for example, 6-O-(6-deoxy- $\alpha$ -L-mannopyranosyl)- $\beta$ -D-glucopyranoside.

On use of the dibenzoylmethane derivatives which are particularly preferred as UV-A filters in combination with the compounds of the formula I,

20 an additional advantage arises: the UV-sensitive dibenzoylmethane derivatives are additionally stabilised by the presence of the compounds of the formula I. The present invention therefore furthermore relates to the use of the compounds of the formula I for the stabilisation of dibenzoylmethane derivatives in preparations.

25 In principle, all known UV filters are suitable for combination with dibenzoylmethane derivatives and with the compounds of the formula I according to the invention, for example one or more additional hydrophilic or lipophilic sun-protection filters which are effective in the UV-A region and/or UV-B region and/or IR and/or VIS region (absorbers). These

30 additional filters can be selected, in particular, from cinnamic acid

- derivatives, salicylic acid derivatives, camphor derivatives, triazine derivatives,  $\beta,\beta$ -diphenyl acrylate derivatives, p-aminobenzoic acid derivatives and polymeric filters and silicone filters, which are described in the application WO 93/04665. Further examples of organic filters are indicated in Patent Application EP-A 0 487 404. Particular preference is given to UV filters whose physiological acceptability has already been demonstrated. Both for UVA and UVB filters, there are many proven substances which are known from the specialist literature, for example
- benzylidenecamphor derivatives, such as 3-(4'-methylbenzylidene)-dl-camphor (for example Eusolex<sup>®</sup> 6300), 3-benzylidenecamphor (for example Mexoryl<sup>®</sup> SD), polymers of N-[(2 and 4)-[(2-oxoborn-3-ylidene)methyl]-benzyl]acrylamide (for example Mexoryl<sup>®</sup> SW), N,N,N-trimethyl-4-(2-oxoborn-3-ylidenemethyl)anilinium methylsulfate (for example Mexoryl<sup>®</sup> SK) or (2-oxoborn-3-ylidene)toluene-4-sulfonic acid (for example Mexoryl<sup>®</sup> SL),
- benzoyl- or dibenzoylmethanes, such as 1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)propane-1,3-dione (for example Eusolex<sup>®</sup> 9020) or 4-isopropylidibenzoylmethane (for example Eusolex<sup>®</sup> 8020),
- benzophenones, such as 2-hydroxy-4-methoxybenzophenone (for example Eusolex<sup>®</sup> 4360) or 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid and its sodium salt (for example Uvinul<sup>®</sup> MS-40),
- methoxycinnamic acid esters, such as octyl methoxycinnamate (for example Eusolex<sup>®</sup> 2292), isopentyl 4-methoxycinnamate, for example as a mixture of the isomers (for example Neo Heliopan<sup>®</sup> E 1000),
- salicylate derivatives, such as 2-ethylhexyl salicylate (for example Eusolex<sup>®</sup> OS), 4-isopropylbenzyl salicylate (for example Megasol<sup>®</sup>) or 3,3,5-trimethylcyclohexyl salicylate (for example Eusolex<sup>®</sup> HMS),

4-aminobenzoic acid and derivatives, such as 4-aminobenzoic acid,  
2-ethylhexyl 4-(dimethylamino)benzoate (for example Eusolex<sup>®</sup> 6007) or  
ethoxylated ethyl 4-aminobenzoate (for example Uvinul<sup>®</sup> P25),

5

phenylbenzimidazolesulfonic acids, such as 2-phenylbenzimidazole-5-  
sulfonic acid and potassium, sodium and triethanolamine salts thereof (for  
example Eusolex<sup>®</sup> 232), 2,2-(1,4-phenylene)bisbenzimidazole-4,6-disul-  
fonic acid and salts thereof (for example Neoheliopan<sup>®</sup> AP) or 2,2-(1,4-  
phenylene)bisbenzimidazole-6-sulfonic acid;

10

and further substances, such as

- 2-ethylhexyl 2-cyano-3,3-diphenylacrylate (for example Eusolex<sup>®</sup> OCR),
- 3,3'-(1,4-phenylenedimethylene)bis(7,7-dimethyl-2-oxobicyclo[2.2.1]hept-  
1-ylmethanesulfonic acid and salts thereof (for example Mexoryl<sup>®</sup> SX),
- 2,4,6-trianilino-(p-carbo-2'-ethylhexyl-1'-oxy)-1,3,5-triazine (for example  
Uvinul<sup>®</sup> T 150) and
- hexyl 2-(4-diethylamino-2-hydroxybenzoyl)benzoate (for example Uvinul<sup>®</sup>  
UVA Plus, BASF).

15

20

The compounds mentioned in the list should only be regarded as exam-  
ples. It is of course also possible to use other UV filters. In particular  
organic particular UV filters, as described in WO 99/66896, can be  
advantageously used in formulations comprising antimicrobial pigments  
according to the present invention.

25

These organic UV filters are generally incorporated into cosmetic formula-  
tions in an amount of from 0.5 to 10 per cent by weight, preferably 1 – 8%.

30

Further suitable organic UV filters are, for example,

- 2-(2H-benzotriazol-2-yl)-4-methyl-6-(2-methyl-3-(1,3,3,3-tetramethyl-1-(trimethylsilyloxy)disiloxanyl)propyl)phenol (for example Silatrizole<sup>®</sup>),
- 2-ethylhexyl 4,4'-[(6-[4-((1,1-dimethylethyl)aminocarbonyl)phenylamino]-1,3,5-triazine-2,4-diyl)diimino]bis(benzoate) (for example Uvasorb<sup>®</sup> HEB),
- $\alpha$ -(trimethylsilyl)- $\omega$ -[trimethylsilyl]oxy]poly[oxy(dimethyl [and about 6% of methyl[2-[p-[2,2-bis(ethoxycarbonyl)vinyl]phenoxy]-1-methyleneethyl] and approximately 1.5% of methyl[3-[p-[2,2-bis(ethoxycarbonyl)vinyl]phenoxy]propenyl] and from 0.1 to 0.4% of (methylhydrogen)silylene]] (n  $\approx$  60) (CAS No. 207 574-74-1)
- 2,2'-methylenebis(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)-phenol) (CAS No. 103 597-45-1)
- 2,2'-(1,4-phenylene)bis(1H-benzimidazole-4,6-disulfonic acid, mono-sodium salt) (CAS No. 180 898-37-7),
- 2,4-bis{[4-(2-ethylhexyloxy)-2-hydroxy]phenyl}-6-(4-methoxyphenyl)-1,3,5-triazine (CAS No. 103 597-45-, 187 393-00-6) and
- 4,4'-[(6-[4-((1,1-dimethylethyl)aminocarbonyl)phenylamino]-1,3,5-triazine-2,4-diyl)diimino]bis(benzoic acid-2-ethylhexylester) (for example Uvasorb<sup>®</sup> HEB).

Further suitable UV filters are methoxyflavones corresponding to the earlier German patent application DE 10232595.2.

Organic UV filters are generally incorporated into cosmetic formulations in an amount of from 0.5 to 20 per cent by weight, preferably 1 – 15%. It may furthermore be preferred in accordance with the invention for the preparations to comprise further inorganic UV filters. Preference is given here both to those from the group consisting of titanium dioxides, such as, for example, coated titanium dioxide (for example Eusolex<sup>®</sup> T-2000 or Eusolex<sup>®</sup> T-AQUA), zinc oxides (for example Sachtotec<sup>®</sup>), iron oxides and also cerium oxides. These inorganic UV filters are generally incorporated



into cosmetic preparations in an amount of from 0.5 to 20 per cent by weight, preferably 2-10%. In particular, it may be preferred here for a UV-Filter to be incorporated into one phase of emulsions and a further inorganic UV filter to be incorporated into the other phase.

5

Preferred compounds having UV-filtering properties are 3-(4'-methylbenzylidene)-dl-camphor, 1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)propane-1,3-dione, 4-isopropylidibenzoylmethane, 2-hydroxy-4-methoxybenzophenone, octyl methoxycinnamate, 3,3,5-trimethylcyclohexyl salicylate, 2-ethylhexyl 4-(dimethylamino)benzoate, 2-ethylhexyl 2-cyano-3,3-diphenylacrylate, 2-phenylbenzimidazole-5-sulfonic acid and its potassium, sodium and tri-ethanolamine salts.

10

Combining one or more compounds of the above-mentioned UV filters can optimise the protective action against the damaging effects of UV radiation.

15

Optimised compositions may comprise, for example, the combination of the organic UV filters 4'-methoxy-6-hydroxyflavone with 1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)propane-1,3-dione and 3-(4'-methylbenzylidene)-dl-camphor. This combination gives rise to broad-band protection, which can be supplemented by the addition of inorganic UV filters, such as titanium dioxide microparticles.

20

All the said UV filters can also be employed in encapsulated form. In particular, it is advantageous to employ organic UV filters in encapsulated form. In detail, the following advantages arise:

25

- The hydrophilicity of the capsule wall can be set independently of the solubility of the UV filter. Thus, for example, it is also possible to incorporate hydrophobic UV filters into purely aqueous preparations. In addition, the oily impression on application of the preparation comprising hydro-

30

phobic UV filters, which is frequently regarded as unpleasant, is suppressed.

5       - Certain UV filters, in particular dibenzoylmethane derivatives, exhibit only reduced photostability in cosmetic preparations. Encapsulation of these filters or compounds which impair the photostability of these filters, such as, for example, cinnamic acid derivatives, enables the photostability of the entire preparation to be increased.

10       - Skin penetration by organic UV filters and the associated potential for irritation on direct application to the human skin is repeatedly being discussed in the literature. The encapsulation of the corresponding substances which is proposed here suppresses this effect.

15       - In general, encapsulation of individual UV filters or other ingredients enables preparation problems caused by the interaction of individual preparation constituents with one another, such as crystallisation processes, precipitation and agglomerate formation, to be avoided since the interaction is suppressed.

20       It is therefore preferred in accordance with the invention for one or more of the UV filters to be in encapsulated form. It is advantageous here for the capsules to be so small that they cannot be viewed with the naked eye. In order to achieve the above-mentioned effects, it is furthermore necessary  
25       for the capsules to be sufficiently stable and the encapsulated active ingredient (UV filter) only to be released to the environment to a small extent, or not at all.

30       Suitable capsules can have walls of inorganic or organic polymers. For example, US 6,242,099 B1 describes the production of suitable capsules with walls of chitin, chitin derivatives or polyhydroxylated polyamines. Capsules which can particularly preferably be employed in accordance with

the invention have walls which can be obtained by sol-gel processes, as described in the applications WO 00/09652, WO 00/72806 and WO 00/71084. Preference is again given here to capsules whose walls are built up from silica gel (silica; undefined silicon oxide hydroxide). The production of corresponding capsules is known to the person skilled in the art, for example from the cited patent applications, whose contents expressly also belong to the subject-matter of the present application.

The capsules in preparations according to the invention are preferably present in amounts which ensure that the encapsulated UV filters are present in the preparation in the above-indicated amounts.

In accordance with the invention, the above-mentioned UV filters may also be provided with a surface treatment which reinforces the hydrophilic or hydrophobic properties. Suitable for hydrophobic modification is, for example, a silicone or silane coating.

As is known, the silicones are organosilicon polymers or oligomers having a straight-chain or cyclic, branched or crosslinked structure with various molecular weights which are obtained by polymerisation and/or polycondensation with suitably functionalised silanes and are essentially formed from recurring principal units in which the silicon atoms are linked to one another via oxygen atoms (siloxane bonding), where optionally substituted hydrocarbon groups are bonded directly to the silicon atoms via a carbon atom. The most common hydrocarbon groups are alkyl groups and in particular methyl groups, fluoroalkyl groups, aryl groups and in particular phenyl groups, as well as alkenyl groups and in particular vinyl groups. Further types of group which can be bonded to the siloxane chain either directly or via a hydrocarbon group are, in particular, hydrogen, the halogens and in particular chlorine, bromine or fluorine, the thiols, alkoxy groups, polyoxyalkylene groups (or polyethers) and in particular polyoxyethylene and/or polyoxypropylene, hydroxyl groups or hydroxyalkyl

groups, optionally substituted amino groups, amide groups, acyloxy groups or acyloxyalkyl groups, hydroxyalkylamino groups or aminoalkyl groups, quaternary ammonium groups, amphoteric groups or betaine groups, anionic groups, such as carboxylates, thioglycolates, sulfosuccinates, thiosulfates, phosphates and sulfates, this list of course in no way being restrictive (so-called 'organo-modified' silicones).

For the purposes of the present invention, the term 'silicones' is also intended to include and cover the silanes and in particular the alkylsilanes required for their preparation.

The silicones which are suitable for the present invention and which can be used for sheathing the UV-protection agents are preferably selected from alkylsilanes, polydialkylsiloxanes and polyalkylhydrogenosiloxanes. The silicones are more preferably selected from octyltrimethylsilane, polydimethylsiloxanes and polymethylhydrogenosiloxanes.

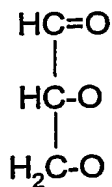
The UV-protection agents may be present in the compositions according to the invention in amounts which are generally in the range from 0.1 to 50% by weight and preferably in amounts which are in the range from 0.5 to 20% by weight, where these amounts are based on the total weight of the composition.

In a further, likewise preferred embodiment of the present invention, the preparation according to the invention comprises at least one self-tanning agent.

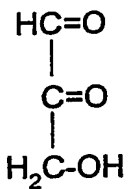
Advantageous self-tanning agents which can be employed are, inter alia:

- 53 -

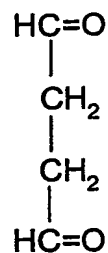
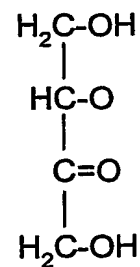
5



glycerol aldehyde

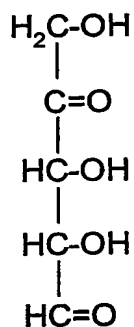


hydroxymethylglyoxal

 $\gamma$ -dialdehyde

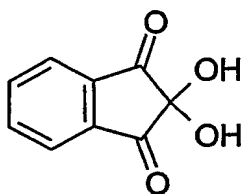
erythrulose

10



15

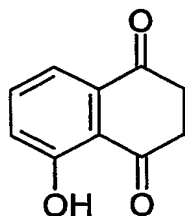
6-aldo-D-fructose



ninhydrin

20

Mention should also be made of 5-hydroxy-1,4-naphthoquinone (juglone), which is extracted from the shells of fresh walnuts

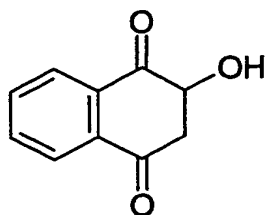


25

5-hydroxy-1,4-naphthoquinone (juglone)

and 2-hydroxy-1,4-naphthoquinone (lawsone), which occurs in henna leaves

30

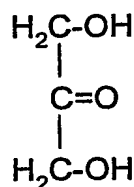


5

2-hydroxy-1,4-naphthoquinone (lawsone).

Very particular preference is given to 1,3-dihydroxyacetone (DHA), a trifunctional sugar which occurs in the human body, and derivatives thereof.

10



15

1,3-dihydroxyacetone (DHA).

The present invention thus furthermore relates to the use of antimicrobial pigments according to the invention in combination with self-tanning agents, in particular dihydroxyacetone or dihydroxyacetone derivatives.

20

Furthermore, the preparations according to the invention may also comprise dyes and coloured pigments that in general do not show any antimicrobial activity. The dyes and coloured pigments can for example be selected from the corresponding positive list in the German Cosmetics Regulation or the EU list of cosmetic colorants. In most cases, they are identical with the dyes approved for foods. Advantageous coloured pigments are, for example, titanium dioxide, mica, iron oxides (for example  $\text{Fe}_2\text{O}_3$ ,  $\text{Fe}_3\text{O}_4$ ,  $\text{FeO}(\text{OH})$ ) and/or tin oxide. Advantageous dyes are, for example, carmine, Berlin Blue, Chromium Oxide Green, Ultramarine Blue and/or Manganese Violet. It is particularly advantageous to select the dyes and/or coloured pigments from the following list. The Colour Index numbers

30

(CINs) are taken from the Rowe Colour Index, 3rd Edition, Society of Dyers and Colourists, Bradford, England, 1971.

	Chemical or other name	CIN	Colour
5	Pigment Green	10006	green
	Acid Green 1	10020	green
	2,4-Dinitrohydroxynaphthalene-7-sulfonic acid	10316	yellow
	Pigment Yellow 1	11680	yellow
	Pigment Yellow 3	11710	yellow
10	Pigment Orange 1	11725	orange
	2,4-Dihydroxyazobenzene	11920	orange
	Solvent Red 3	12010	red
	1-(2'-Chloro-4'-nitro-1'-phenylazo)-2-hydroxynaphthalene	12085	red
	Pigment Red 3	12120	red
	Ceres Red; Sudan Red; Fat Red G	12150	red
	Pigment Red 112	12370	red
15	Pigment Red 7	12420	red
	Pigment Brown 1	12480	brown
	N-(5-chloro-2,4-dimethoxyphenyl)-4-[[5-[(diethylamino)-sulfonyl]-2-methoxyphenyl]azo]-3-hydroxynaphthalene-2-carboxamide	12490	red
	Disperse Yellow 16	12700	yellow
20	1-(4-Sulfo-1-phenylazo)-4-aminobenzene-5-sulfonic acid	13015	yellow
	2,4-Dihydroxy-azobenzene-4'-sulfonic acid	14270	orange
	2-(2,4-Dimethylphenylazo-5-sulfonyl)-1-hydroxynaphthalene-4-sulfonic acid	14700	red
	2-(4-Sulfo-1-naphthylazo)-1-naphthol-4-sulfonic acid	14720	red
	2-(6-Sulfo-2,4-xylylazo)-1-naphthol-5-sulfonic acid	14815	red
	1-(4'-Sulfophenylazo)-2-hydroxynaphthalene	15510	orange
25	1-(2-Sulfonic acid-4-chloro-5-carboxy-1-phenylazo)-2-hydroxynaphthalene	15525	red
	1-(3-Methylphenylazo-4-sulfonyl)-2-hydroxynaphthalene	15580	red
	1-(4', (8')-Sulfonyl)-2-hydroxynaphthalene	15620	red
	2-Hydroxy-1,2'-azonaphthalene-1'-sulfonic acid	15630	red
	3-Hydroxy-4-phenylazo-2-naphthylcarboxylic acid	15800	red
30	1-(2-Sulfo-4-methyl-1-phenylazo)-2-naphthylcarboxylic acid	15850	red

	Chemical or other name	CIN	Colour
	1-(2-Sulfo-4-methyl-5-chloro-1-phenylazo)-2-hydroxy-naphthalene-3-carboxylic acid	15865	red
	1-(2-Sulfo-1-naphthylazo)-2-hydroxynaphthalene-3-carboxylic acid	15880	red
5	1-(3-Sulfo-1-phenylazo)-2-naphthol-6-sulfonic acid	15980	orange
	1-(4-Sulfo-1-phenylazo)-2-naphthol-6-sulfonic acid	15985	yellow
	Allura Red	16035	red
	1-(4-Sulfo-1-naphthylazo)-2-naphthol-3,6-disulfonic acid	16185	red
	Acid Orange 10	16230	orange
	1-(4-Sulfo-1-naphthylazo)-2-naphthol-6,8-disulfonic acid	16255	red
10	1-(4-Sulfo-1-naphthylazo)-2-naphthol-3,6,8-trisulfonic acid	16290	red
	8-Amino-2-phenylazo-1-naphthol-3,6-disulfonic acid	17200	red
	Acid Red 1	18050	red
	Acid Red 155	18130	red
	Acid Yellow 121	18690	yellow
15	Acid Red 180	18736	red
	Acid Yellow 11	18820	yellow
	Acid Yellow 17	18965	yellow
	4-(4-Sulfo-1-phenylazo)-1-(4-sulfophenyl)-5-hydroxy-pyrazolone-3-carboxylic acid	19140	yellow
	Pigment Yellow 16	20040	yellow
20	2,6-(4'-Sulfo-2'',4''-dimethyl)bispheylazo)-1,3-dihydroxy-benzene	20170	orange
	Acid Black 1	20470	black
	Pigment Yellow 13	21100	yellow
	Pigment Yellow 83	21108	yellow
	Solvent Yellow	21230	yellow
	Acid Red 163	24790	red
25	Acid Red 73	27290	red
	2-[4'-(4''-Sulfo-1''-phenylazo)-7'-sulfo-1'-naphthylazo]-1-hydroxy-7-aminonaphthalene-3,6-disulfonic acid	27755	black
	4-[4''-Sulfo-1''-phenylazo)-7'-sulfo-1'-naphthylazo]-1-hydroxy-8-acetylaminonaphthalene-3,5-disulfonic acid	28440	black
	Direct Orange 34, 39, 44, 46, 60	40215	orange
30	Food Yellow	40800	orange
	trans- $\beta$ -Apo-8'-carotene aldehyde (C <sub>30</sub> )	40820	orange
	trans-Apo-8'-carotinic acid (C <sub>30</sub> ) ethyl ester	40850	orange



	Chemical or other name	CIN	Colour
5	Canthaxanthine	40850	orange
	Acid Blue 1	42045	blue
	2,4-Disulfo-5-hydroxy-4'-4''-bis(diethylamino)triphenylcarbinol	42051	blue
	4-[(4-N-Ethyl-p-sulfobenzylamino)-phenyl-(4-hydroxy-2-sulfophenyl)(methylene)-1-(N-ethyl-N-p-sulfobenzyl)-2,5-cyclohexadienimine]	42053	green
	Acid Blue 7	42080	blue
10	(N-Ethyl-p-sulfobenzylamino)phenyl-(2-sulfophenyl)-methylene-(N-ethyl-N-p-sulfobenzyl)- $\Delta^{2,5}$ -cyclohexadienimine	42090	blue
	Acid Green 9	42100	green
	Diethyldisulfobenzyl-di-4-amino-2-chloro-di-2-methyl-fuchsonimmonium	42170	green
	Basic Violet 14	42510	violet
	Basic Violet 2	42520	violet
15	2'-Methyl-4'-(N-ethyl-N-m-sulfobenzyl)amino-4''-(N-diethyl)-amino-2-methyl-N-ethyl-N-m-sulfobenzylfuchsonimmonium	42735	blue
	4'-(N-Dimethyl)amino-4''-(N-phenyl)aminonaphtho-N-dimethylfuchsonimmonium	44045	blue
	2-Hydroxy-3,6-disulfo-4,4'-bisdimethylaminonaphthofuchsonimmonium	44090	green
	Acid Red 52	45100	red
	3-(2'-Methylphenylamino)-6-(2'-methyl-4'-sulfophenylamino)-9-(2''-carboxyphenyl)xanthenium salt	45190	violet
20	Acid Red 50	45220	red
	Phenyl-2-oxyfluorone-2-carboxylic acid	45350	yellow
	4,5-Dibromofluorescein	45370	orange
	2,4,5,7-Tetrabromofluorescein	45380	red
	Solvent Dye	45396	orange
25	Acid Red 98	45405	red
	3',4',5',6'-Tetrachloro-2,4,5,7-tetrabromofluorescein	45410	red
	4,5-Diiodofluorescein	45425	red
	2,4,5,7-Tetraiodofluorescein	45430	red
	Quinophthalone	47000	yellow
30	Quinophthalonedisulfonic acid	47005	yellow
	Acid Violet 50	50325	violet
	Acid Black 2	50420	black

	Chemical or other name	CIN	Colour
5	Pigment Violet 23	51319	violet
	1,2-Dioxyanthraquinone, calcium aluminium complex	58000	red
	3-Oxypyrene-5,8,10-sulfonic acid	59040	green
	1-Hydroxy-4-N-phenylaminoanthraquinone	60724	violet
	1-Hydroxy-4-(4'-methylphenylamino)anthraquinone	60725	violet
10	Acid Violet 23	60730	violet
	1,4-Di(4'-methylphenylamino)anthraquinone	61565	green
	1,4-Bis(o-sulfo-p-toluidino)anthraquinone	61570	green
	Acid Blue 80	61585	blue
	Acid Blue 62	62045	blue
15	N,N'-Dihydro-1,2,1',2'-anthraquinonazine	69800	blue
	Vat Blue 6; Pigment Blue 64	69825	blue
	Vat Orange 7	71105	orange
	Indigo	73000	blue
	Indigodisulfonic acid	73015	blue
20	4,4'-Dimethyl-6,6'-dichlorothioindigo	73360	red
	5,5'-Dichloro-7,7'-dimethylthioindigo	73385	violet
	Quinacridone Violet 19	73900	violet
	Pigment Red 122	73915	red
	Pigment Blue 16	74100	blue
25	Phthalocyanine	74160	blue
	Direct Blue 86	74180	blue
	Chlorinated phthalocyanines	74260	green
	Natural Yellow 6, 19; Natural Red 1	75100	yellow
	Bixin, Nor-Bixin	75120	orange
30	Lycopin	75125	yellow
	trans-alpha-, beta- or gamma-carotene	75130	orange
	Keto and/or hydroxy derivatives of carotene	75135	yellow
	Guanine or pearlescent agent	75170	white
	1,7-Bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione	75300	yellow
30	Complex salt (Na, Al, Ca) of carminic acid	75470	red
	Chlorophyll a and b; copper compounds of chlorophylls and chlorophyllines	75810	green
	Aluminium	77000	white
	Aluminium hydroxide	77002	white
	Water-containing aluminium silicates	77004	white

	Chemical or other name	CIN	Colour
5	Ultramarine	77007	blue
	Pigment Red 101 and 102	77015	red
	Barium sulfate	77120	white
	Bismuth oxychloride and mixtures thereof with mica	77163	white
	Calcium carbonate	77220	white
10	Calcium sulfate	77231	white
	Carbon	77266	black
	Pigment Black 9	77267	black
	Carbo medicinalis vegetabilis	77268	black
		:1	
15	Chromium oxide	77288	green
	Chromium oxide, water-containing	77278	green
	Pigment Blue 28, Pigment Green 14	77346	green
	Pigment Metal 2	77400	brown
	Gold	77480	brown
20	Iron oxides and hydroxides	77489	orange
	Iron oxide	77491	red
	Iron oxide hydrate	77492	yellow
25	Iron oxide	77499	black
	Mixtures of iron(II) and iron(III) hexacyanoferrate	77510	blue
	Pigment White 18	77713	white
	Manganese ammonium diphosphate	77742	violet
	Manganese phosphate; $Mn_3(PO_4)_2 \cdot 7 H_2O$	77745	red
30	Silver	77820	white
	Titanium dioxide and mixtures thereof with mica	77891	white
	Zinc oxide	77947	white
	6,7-Dimethyl-9-(1'-D-ribityl)isoalloxazine, lactoflavin		yellow
	Sugar dye		brown
35	Capsanthin, capsorubin		orange
	Betanin		red
	Benzopyrylium salts, anthocyanins		red
	Aluminium, zinc, magnesium and calcium stearate		white
	Bromothymol Blue		blue

30 It may furthermore be favourable to select, as dye, one or more substances from the following group:

2,4-dihydroxyazobenzene, 1-(2'-chloro-4'-nitro-1'-phenylazo)-2-hydroxy-naphthalene, Ceres Red, 2-(4-sulfo-1-naphthylazo)-1-naphthol-4-sulfonic acid, the calcium salt of 2-hydroxy-1,2'-azonaphthalene-1'-sulfonic acid, the calcium and barium salts of 1-(2-sulfo-4-methyl-1-phenylazo)-2-naphthyl-carboxylic acid, the calcium salt of 1-(2-sulfo-1-naphthylazo)-2-hydroxy-naphthalene-3-carboxylic acid, the aluminium salt of 1-(4-sulfo-1-phenylazo)-2-naphthol-6-sulfonic acid, the aluminium salt of 1-(4-sulfo-1-naphthylazo)-2-naphthol-3,6-disulfonic acid, 1-(4-sulfo-1-naphthylazo)-2-naphthol-6,8-disulfonic acid, the aluminium salt of 4-(4-sulfo-1-phenylazo)-2-(4-sulfophenyl)-5-hydroxypyrazolone-3-carboxylic acid, the aluminium and zirconium salts of 4,5-dibromofluorescein, the aluminium and zirconium salts of 2,4,5,7-tetrabromofluorescein, 3',4',5',6'-tetrachloro-2,4,5,7-tetrabromofluorescein and its aluminium salt, the aluminium salt of 2,4,5,7-tetraiodofluorescein, the aluminium salt of quinophthalonedisulfonic acid, the aluminium salt of indigodisulfonic acid, red and black iron oxide (CIN: 77 491 (red) and 77 499 (black)), iron oxide hydrate (CIN: 77492), manganese ammonium diphosphate and titanium dioxide.

Also advantageous are oil-soluble natural dyes, such as, for example, paprika extract,  $\beta$ -carotene or cochineal.

Also advantageous for the purposes of the present invention are gel creams comprising effect pigments. Particular preference is given to the types of effect pigment listed below:

1. Natural effect pigments, such as, for example,
  - a) "pearl essence" (guanine/hypoxanthine mixed crystals from fish scales) and
  - b) "mother of pearl" (ground mussel shells)
2. Monocrystalline effect pigments, such as, for example, bismuth oxychloride (BiOCl)
3. Layered substrate pigments: for example mica/metal oxide

The basis for effect pigments is formed by, for example, pulverulent pigments or castor oil dispersions of bismuth oxychloride and/or titanium dioxide as well as bismuth oxychloride and/or titanium dioxide on mica. The lustre pigment listed under CIN 77163, for example, is particularly advantageous.

Also advantageous are, for example, the following effect pigment types based on mica/metal oxide:

10

Group	Coating/layer thickness	Colour
<b>Silver-white effect pigments</b>	TiO <sub>2</sub> : 40-60 nm	silver
<b>Interference pigments</b>	TiO <sub>2</sub> : 60-80 nm	yellow
	TiO <sub>2</sub> : 80-100 nm	red
	TiO <sub>2</sub> : 100-140 nm	blue
	TiO <sub>2</sub> : 120-160 nm	green
<b>Coloured lustre pigments</b>	Fe <sub>2</sub> O <sub>3</sub>	bronze
	Fe <sub>2</sub> O <sub>3</sub>	copper
	Fe <sub>2</sub> O <sub>3</sub>	red
	Fe <sub>2</sub> O <sub>3</sub>	red-violet
	Fe <sub>2</sub> O <sub>3</sub>	red-green
	Fe <sub>2</sub> O <sub>3</sub>	black
<b>Combination pigments</b>	TiO <sub>2</sub> / Fe <sub>2</sub> O <sub>3</sub>	gold shades
	TiO <sub>2</sub> / Cr <sub>2</sub> O <sub>3</sub>	green
	TiO <sub>2</sub> / Berlin Blue	dark blue

15

20

25

Particular preference is given to, for example, the pearlescent pigments available from Merck KGaA under the trade names Timiron<sup>®</sup>, Colorona<sup>®</sup> or Dichrona<sup>®</sup>.

30

The list of the said effect pigments is of course not intended to be limiting. Effect pigments which are advantageous for the purposes of the present invention can be obtained by numerous routes known per se. In addition, other substrates apart from mica can also, for example, be coated with further metal oxides, such as, for example, silica and the like. For example,

TiO<sub>2</sub>- and Fe<sub>2</sub>O<sub>3</sub>-coated SiO<sub>2</sub> particles ("Ronasphere" grades), which are marketed by Merck KGaA and are particularly suitable for the optical reduction of fine wrinkles, are advantageous.

5 It may additionally be advantageous to completely omit a substrate such as mica. Particular preference is given to effect pigments prepared using SiO<sub>2</sub>. Such pigments, which may additionally also have goniochromatic effects, are available, for example, from BASF under the trade name Sicopearl<sup>®</sup> Fantastico.

10 It may also be advantageous to employ Engelhard pigments based on calcium sodium borosilicate coated with titanium dioxide. These are available under the name Reflecks<sup>®</sup>. Due to their particle size of 40-80 µm, they have a glitter effect in addition to the colour.

15 Also particularly advantageous are effect pigments available from Flora Tech under the trade name Metasomes<sup>®</sup> Standard/Glitter in various colours (yellow, red, green and blue). The glitter particles here are in the form of mixtures with various assistants and dyes (such as, for example, the dyes  
20 with the colour index (CI) numbers 19140, 77007, 77289 and 77491).

The dyes and pigments can be in individual form or in the form of a mixture and mutually coated with one another, with different colour effects generally being caused by different coating thicknesses. The total amount  
25 of dyes and colouring pigments is advantageously selected from the range from, for example, 0.1% by weight to 30% by weight, preferably from 0.5 to 15% by weight, in particular from 1.0 to 10% by weight, in each case based on the total weight of the preparations.

30 Furthermore it is preferred to combine antimicrobial pigments according to the present invention with antioxidant properties of antioxidants. Another subject-matter of the present invention is therefore a preparation having

antioxidant properties comprising at least one antioxidant, for example a compound of the formula I as described above. These compounds can be used as antioxidants as well as UV filters.

- 5 Preference is therefore also given to preparations comprising at least one compound of the formula I which is characterised in that at least two adjacent radicals of the radicals  $R^1$  to  $R^4$  are OH and at least two adjacent radicals of the radicals  $R^5$  to  $R^7$  are OH.
- 10 Particularly preferred preparations comprise at least one compound of the formula I which is characterised in that at least three adjacent radicals of the radicals  $R^1$  to  $R^4$  are OH, preferably with the radicals  $R^1$  to  $R^3$  being OH.
- 15 In order that the compounds of the formula I are able to develop their positive action as free-radical scavengers on the skin particularly well, it may be preferred to allow the compounds of the formula I to penetrate into deeper skin layers. Several possibilities are available for this purpose. Firstly, the compounds of the formula I can have an adequate lipophilicity in
- 20 order to be able to penetrate through the outer skin layer into epidermal layers. As a further possibility, corresponding transport agents, for example liposomes, which enable transport of the compounds of the formula I through the outer skin layers may also be provided in the preparation. Finally, systemic transport of the compounds of the formula I is also conceivable. The preparation is then designed, for example, in such a way that
- 25 it is suitable for oral administration.

In general, the substances of the formula I act as free-radical scavengers. Free radicals of this type are not generated only by sunlight, but instead are

30 formed under various conditions. Examples are anoxia, which blocks the flow of electrons upstream of the cytochrome oxidases and causes the formation of superoxide free-radical anions; inflammation associated, inter

alia, with the formation of superoxide anions by the membrane NADPH oxidase of the leucocytes, but also associated with the formation (through disproportionation in the presence of iron(II) ions) of the hydroxyl free radicals and other reactive species which are normally involved in the phenomenon of phagocytosis; and lipid autooxidation, which is generally initiated by a hydroxyl free radical and produces lipidic alkoxy free radicals and hydroperoxides.

It is assumed that the preferred compounds of the formula I also act as enzyme inhibitors. They presumably inhibit histidine decarboxylase, protein kinases, elastase, aldose reductase and hyaluronidase, and therefore enable the intactness of the basic substance of vascular sheaths to be maintained. Furthermore, they presumably inhibit non-specifically catechol O-methyl transferase, causing the amount of available catecholamine and thus the vascular strength to be increased. Furthermore, they inhibit AMP phosphodiesterase, giving the substances potential for inhibiting thrombocyte aggregation.

Owing to these properties, the preparations according to the invention are, in general, suitable for immune protection and for the protection of DNA and RNA. In particular, the preparations are suitable for the protection of DNA and RNA against oxidative attack, against free radicals and against damage due to radiation, in particular UV radiation. A further advantage of the preparations according to the invention is cell protection, in particular protection of Langerhans cells against damage due to the above-mentioned influences. All these uses and the use of the compounds of the formula I for the preparation of preparations which can be employed correspondingly are expressly also a subject-matter of the present invention.

Of the phenols having an antioxidative action, the polyphenols, some of which are naturally occurring, are of particular interest for applications in the pharmaceutical, cosmetic or nutrition sector. For example, the flavon-



- oids or bioflavonoids, which are principally known as plant dyes, frequently have an antioxidant potential. K. Lemanska, H. Szymusiak, B. Tyrakowska, R. Zielinski, I.M.C.M. Rietjens; Current Topics in Biophysics 2000, 24(2), 101-108, are concerned with effects of the substitution pattern of mono- and dihydroxyflavones. It is observed therein that dihydroxyflavones containing an OH group adjacent to the keto function or OH groups in the 3',4'- or 6,7- or 7,8-position have antioxidative properties, while other mono- and dihydroxyflavones in some cases do not have antioxidative properties.
- Quercetin (cyanidanol, cyanidenolon 1522, meletin, sophoretin, ericin, 3,3',4',5,7-pentahydroxyflavone) is frequently mentioned as a particularly effective antioxidant (for example C.A. Rice-Evans, N.J. Miller, G. Paganga, Trends in Plant Science 1997, 2(4), 152-159). K. Lemanska, H. Szymusiak, B. Tyrakowska, R. Zielinski, A.E.M.F. Soffers, I.M.C.M. Rietjens; Free Radical Biology & Medicine 2001, 31(7), 869-881, have investigated the pH dependence of the antioxidant action of hydroxyflavones. Quercetin exhibits the greatest activity amongst the structures investigated over the entire pH range.
- For the purposes of the invention, the term flavone derivatives is taken to mean flavonoids and coumaranones. For the purposes of the invention, the term flavonoids is taken to mean the glycosides of flavonones, flavones, 3-hydroxyflavones (= flavonols), aurones, isoflavones and rotenoids [Römpf Chemie Lexikon [Römpf's Lexicon of Chemistry], Volume 9, 1993]. For the purposes of the present invention, however, this is also taken to mean the aglycones, i.e. the sugar-free constituents, and flavonoid and aglycone derivatives. For the purposes of the present invention, the term flavonoid is furthermore also taken to mean anthocyanidine (cyanidine). For the purposes of the present invention, the term coumaranones is also taken to mean derivatives thereof.

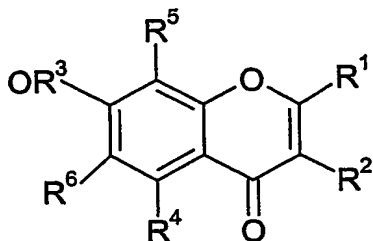
Preferred flavonoids are derived from flavonones, flavones, 3-hydroxy-flavones, aurones and isoflavones, in particular from flavonones, flavones, 3-hydroxyflavones and aurones.

- 5 The flavonoids are preferably selected from the following compounds:  
 4,6,3',4'-tetrahydroxyaurone, quercetin, rutin, isoquercetin, eriodictyol, taxifolin, luteolin, trishydroxyethylquercetin (troxequercetin), trishydroxyethylrutin (troxerutin), trishydroxyethylisoquercetin (troxeisoquercetin),  
 10 trishydroxyethyluteolin (troxeluteolin),  $\alpha$ -glycosylrutin, tiliroside and sulfates and phosphates thereof. Of the flavonoids, particular preference is given to rutin, tiliroside,  $\alpha$ -glycosylrutin and troxerutin as active compounds according to the invention.

- 15 Of the coumaranones, 4,6,3',4'-tetrahydroxybenzyl-3-coumaranone is preferred.

- The term chromone derivatives is preferably taken to mean certain chromen-2-one derivatives which are suitable as active ingredients for the preventative treatment of human skin and human hair against ageing  
 20 processes and harmful environmental influences. At the same time, they exhibit a low irritation potential for the skin, have a positive effect on water binding in the skin, maintain or increase the elasticity of the skin and thus promote smoothing of the skin. These compounds preferably conform to the formula II

25



II

30

where

- 67 -

R<sup>1</sup> and R<sup>2</sup> may be identical or different and are selected from

- H, -C(=O)-R<sup>7</sup>, -C(=O)-OR<sup>7</sup>,

- straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-alkyl groups,

- straight-chain or branched C<sub>3</sub>- to C<sub>20</sub>-alkenyl groups,

5 - straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-hydroxyalkyl groups, where the hydroxyl group can be bonded to a primary or secondary carbon atom in the chain and furthermore the alkyl chain may also be interrupted by oxygen, and/or

- C<sub>3</sub>- to C<sub>10</sub>-cycloalkyl groups and/or C<sub>3</sub>- to C<sub>12</sub>-cycloalkenyl groups,

10 where the rings may each also be bridged by -(CH<sub>2</sub>)<sub>n</sub>- groups, where n = 1 to 3,

R<sup>3</sup> is H or straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-alkyl groups,

R<sup>4</sup> is H or OR<sup>8</sup>,

R<sup>5</sup> and R<sup>6</sup> may be identical or different and are selected from

15 - -H, -OH,

- straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-alkyl groups,

- straight-chain or branched C<sub>3</sub>- to C<sub>20</sub>-alkenyl groups,

20 - straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-hydroxyalkyl groups, where the hydroxyl group can be bonded to a primary or secondary carbon atom in the chain and furthermore the alkyl chain may also be interrupted by oxygen, and

R<sup>7</sup> is H, straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-alkyl groups, a polyhydroxy compound, such as preferably an ascorbic acid radical or glycosidic radicals, and

25 R<sup>8</sup> is H or straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-alkyl groups, where at least 2 of the substituents R<sup>1</sup>, R<sup>2</sup> and R<sup>4</sup>-R<sup>6</sup> are not H or at least one substituent from R<sup>1</sup> and R<sup>2</sup> is -C(=O)-R<sup>7</sup> or -C(=O)-OR<sup>7</sup>.

30 The proportion of one or more compounds selected from flavonoids, chromone derivatives and coumaranones in the preparation according to the invention is preferably from 0.001 to 5% by weight, particularly preferably from 0.01 to 2% by weight, based on the preparation as a whole.

As already described, preferred compositions according to the invention are also suitable for the treatment of skin diseases associated with a defect in keratinisation which affects differentiation and cell proliferation, in particular for the treatment of acne vulgaris, acne comedonica, polymorphic  
5 acne, acne rosaceae, nodular acne, acne conglobata, age-induced acne, acne which arises as a side effect, such as acne solaris, medicament-induced acne or acne professionalis, for the treatment of other defects in keratinisation, in particular ichthyosis, ichthyosiform states, Darier's  
10 disease, keratosis palmoplantaris, leucoplasia, leucoplasiform states, herpes of the skin and mucous membrane (buccal) (lichen), for the treatment of other skin diseases associated with a defect in keratinisation and which have an inflammatory and/or immunoallergic component and in particular all forms of psoriasis which affect the skin, mucous membranes  
15 and fingers and toenails, and psoriatic rheumatism and skin atopia, such as eczema or respiratory atopia, or hypertrophy of the gums, it furthermore being possible for the compounds to be used for some inflammations which are not associated with a defect in keratinisation, for the treatment of all benign or malignant excrescence of the dermis or epidermis, which may be  
20 of viral origin, such as verruca vulgaris, verruca plana, epidermodysplasia verruciformis, oral papillomatosis, papillomatosis florida, and excrescence which may be caused by UV radiation, in particular epithelioma baso-cellulare and epithelioma spinocellulare, for the treatment of other skin diseases, such as dermatitis bullosa and diseases affecting the collagen, for  
25 the treatment of certain eye diseases, in particular corneal diseases, for overcoming or combating light-induced skin ageing associated with ageing, for reducing pigmentation and keratosis actinica and for the treatment of all diseases associated with normal ageing or light-induced ageing, for the prevention or healing of wounds/scars of atrophie of the epidermis and/or  
30 dermis caused by locally or systemically applied corticosteroids and all other types of skin atrophie, for the prevention or treatment of defects in wound healing, for the prevention or elimination of stretch marks caused by

pregnancy or for the promotion of wound healing, for combating defects in  
tallow production, such as hyperseborrhoea in acne or simple seborrhoea,  
for combating or preventing cancer-like states or pre-carcinogenic states, in  
particular promyelocytic leukaemia, for the treatment of inflammatory  
5 diseases, such as arthritis, for the treatment of all virus-induced diseases of  
the skin or other areas of the body, for the prevention or treatment of  
alopecia, for the treatment of skin diseases or diseases of other areas of  
the body with an immunological component, for the treatment of  
cardiovascular diseases, such as arteriosclerosis or hypertension, and of  
10 non-insulin-dependent diabetes, and for the treatment of skin problems  
caused by UV radiation.

The protective action against oxidative stress or against the effect of free  
radicals can thus be further improved if the preparations comprise one or  
15 more further antioxidants. The person skilled in the art being presented with  
absolutely no difficulties in selecting suitably fast-acting or time-delayed  
antioxidants.

In a preferred embodiment of the present invention, the preparation is  
20 therefore a preparation for the protection of body cells against oxidative  
stress, in particular for reducing skin ageing, characterised in that it pref-  
erably comprises one or more further antioxidants besides the one or more  
compounds of the formula I.

25 There are many proven substances known from the specialist literature  
which also can be used as antioxidants, for example amino acids (for  
example glycine, histidine, tyrosine, tryptophan) and derivatives thereof,  
imidazoles (for example urocanic acid) and derivatives thereof, peptides,  
such as D,L-carnosine, D-carnosine, L-carnosine and derivatives thereof  
30 (for example anserine), carotinoids, carotenes (for example  $\alpha$ -carotene,  $\beta$ -  
carotene, lycopene) and derivatives thereof, chlorogenic acid and

derivatives thereof, lipoic acid and derivatives thereof (for example dihydrolipoic acid), aurothioglucose, propylthiouracil and other thiols (for example thioredoxin, glutathione, cysteine, cystine, cystamine and the glycosyl, N-acetyl, methyl, ethyl, propyl, amyl, butyl and lauryl, palmitoyl, 5 oleyl,  $\gamma$ -linoleyl, cholesteryl and glyceryl esters thereof) and salts thereof, dilauryl thiodipropionate, distearyl thiodipropionate, thiodipropionic acid and derivatives thereof (esters, ethers, peptides, lipids, nucleotides, nucleosides and salts), and sulfoximine compounds (for example buthionine sulfoximines, homocysteine sulfoximine, buthionine sulfones, penta-, hexa- 10 and heptathionine sulfoximine) in very low tolerated doses (for example pmol to  $\mu$ mol/kg), and also (metal) chelating agents (for example  $\alpha$ -hydroxy fatty acids, palmitic acid, phytic acid, lactoferrin),  $\alpha$ -hydroxy acids (for example citric acid, lactic acid, malic acid), humic acid, bile acid, bile extracts, bilirubin, biliverdin, EDTA, EGTA and derivatives thereof, 15 unsaturated fatty acids and derivatives thereof, vitamin C and derivatives (for example ascorbyl palmitate, magnesium ascorbyl phosphate, ascorbyl acetate), tocopherols and derivatives (for example vitamin E acetate), vitamin A and derivatives (for example vitamin A palmitate), and coniferyl benzoate of benzoin resin, rutinic acid and derivatives thereof,  $\alpha$ -glycosyl rutin, ferulic acid, furfurylidene-glucitol, carnosine, butylhydroxytoluene, 20 butylhydroxyanisole, nordihydroguaiaretic acid, trihydroxybutyrophenone, quercetin, uric acid and derivatives thereof, mannose and derivatives thereof, zinc and derivatives thereof (for example ZnO, ZnSO<sub>4</sub>), selenium and derivatives thereof (for example selenomethionine), stilbenes and 25 derivatives thereof (for example stilbene oxide, trans-stilbene oxide).

Mixtures of antioxidants are likewise suitable for use in the cosmetic preparations according to the invention. Known and commercial mixtures are, for example, mixtures comprising, as active ingredients, lecithin, L-(+)- 30 ascorbyl palmitate and citric acid (for example Oxydex<sup>®</sup> AP), natural tocopherols, L-(+)-ascorbyl palmitate, L-(+)-ascorbic acid and citric acid (for

- example Oxy<sup>®</sup>nex K LIQUID), tocopherol extracts from natural sources, L-(+)-ascorbyl palmitate, L-(+)-ascorbic acid and citric acid (for example Oxy<sup>®</sup>nex L LIQUID), DL- $\alpha$ -tocopherol, L-(+)-ascorbyl palmitate, citric acid and lecithin (for example Oxy<sup>®</sup>nex LM) or butylhydroxytoluene (BHT), L-(+)-ascorbyl palmitate and citric acid (for example Oxy<sup>®</sup>nex 2004). Antioxidants of this type are usually employed with compounds of the formula I in compositions of this type in ratios in the range from 1000:1 to 1:1000, preferably in amounts of from 100:1 to 1:100.
- 10 The preparations according to the invention may comprise vitamins as further ingredients. The preparations according to the invention preferably comprise vitamins and vitamin derivatives selected from vitamin A, vitamin A propionate, vitamin A palmitate, vitamin A acetate, retinol, vitamin B, thiamine chloride hydrochloride (vitamin B<sub>1</sub>), riboflavin (vitamin B<sub>2</sub>),  
15 nicotinamide, vitamin C (ascorbic acid), vitamin D, ergocalciferol (vitamin D<sub>2</sub>), vitamin E, DL- $\alpha$ -tocopherol, tocopherol E acetate, tocopherol hydrogensuccinate, vitamin K<sub>1</sub>, esculin (vitamin P active ingredient), thiamine (vitamin B<sub>1</sub>), nicotinic acid (niacin), pyridoxine, pyridoxal, pyridoxamine, (vitamin B<sub>6</sub>), pantothenic acid, biotin, folic acid and cobalamine  
20 (vitamin B<sub>12</sub>), particularly preferably vitamin A palmitate, vitamin C and derivatives thereof, DL- $\alpha$ -tocopherol, tocopherol E acetate, nicotinic acid, pantothenic acid and biotin. Vitamins are usually employed here with compounds of the formula I in ratios in the range from 1000:1 to 1:1000, preferably in amounts of from 100:1 to 1:100.
- 25 The preparations according to the invention may in addition comprise further conventional skin-protecting or skin-care active ingredients. These may in principle be any active ingredients known to the person skilled in the art.
- 30 Particularly preferred active ingredients are pyrimidinecarboxylic acids and/or aryl oximes.

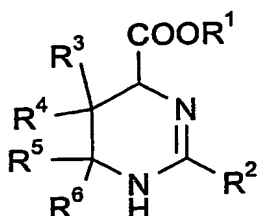
Pyrimidinecarboxylic acids occur in halophilic microorganisms and play a role in osmoregulation of these organisms (*E.A. Galinski et al., Eur. J. Biochem., 149 (1985) pages 135-139*). Of the pyrimidinecarboxylic acids, particular mention should be made here of ectoin ((S)-1,4,5,6-tetrahydro-2-methyl-4-pyrimidinecarboxylic acid) and hydroxyectoin ((S,S)-1,4,5,6-tetrahydro-5-hydroxy-2-methyl-4-pyrimidinecarboxylic acid) and derivatives thereof. These compounds stabilise enzymes and other biomolecules in aqueous solutions and organic solvents. Furthermore, they stabilise, in particular, enzymes against denaturing conditions, such as salts, extreme pH values, surfactants, urea, guanidinium chloride and other compounds.

Ectoin and ectoin derivatives, such as hydroxyectoin, can advantageously be employed in medicaments. In particular, hydroxyectoin can be employed for the preparation of a medicament for the treatment of skin diseases. Other areas of application of hydroxyectoin and other ectoin derivatives are typically in areas in which, for example, trehalose is used as additive. Thus, ectoin derivatives, such as hydroxyectoin, can be used as protectant in dried yeast and bacteria cells. Pharmaceutical products, such as non-glycosylated, pharmaceutically active peptides and proteins, for example t-PA, can also be protected with ectoin or its derivatives.

Of the cosmetic applications, particular mention should be made of the use of ectoin and ectoin derivatives for the care of aged, dry or irritated skin. Thus, European Patent Application EP-A-0 671 161 describes, in particular, that ectoin and hydroxyectoin are employed in cosmetic preparations, such as powders, soaps, surfactant-containing cleansing products, lipsticks, rouge, make-ups, care creams and sunscreen preparations.

Preference is given here to the use of a pyrimidinecarboxylic acid of the following formula III





III

5

in which R<sup>1</sup> is a radical H or C1-8-alkyl, R<sup>2</sup> is a radical H or C1-4-alkyl, and R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are each, independently of one another, a radical from the group consisting of H, OH, NH<sub>2</sub> and C1-4-alkyl. Preference is given to the use of pyrimidinecarboxylic acids in which R<sup>2</sup> is a methyl or ethyl group, and R<sup>1</sup> or R<sup>5</sup> and R<sup>6</sup> are H. Particular preference is given to the use of the pyrimidinecarboxylic acids ectoin ((S)-1,4,5,6-tetrahydro-2-methyl-4-pyrimidinecarboxylic acid) and hydroxyectoin ((S,S)-1,4,5,6-tetrahydro-5-hydroxy-2-methyl-4-pyrimidinecarboxylic acid). The preparations according to the invention preferably comprise pyrimidinecarboxylic acids of this type in amounts of up to 15% by weight. In combination with compounds of formula I, the pyrimidinecarboxylic acids are preferably employed in ratios of from 100:1 to 1:100 with respect to the compounds of the formula I, with ratios in the range from 1:10 to 10:1 being particularly preferred.

20

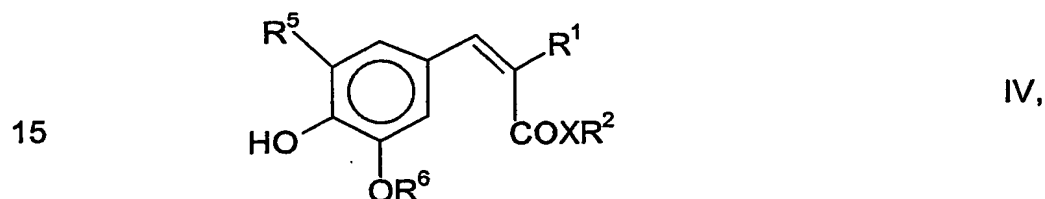
Of the aryl oximes, preference is given to the use of 2-hydroxy-5-methyl-laurophenone oxime, which is also known as HMLO, LPO or F5. Its suitability for use in cosmetic compositions is disclosed, for example, in DE-A-41 16 123. Preparations which comprise 2-hydroxy-5-methyl-laurophenone oxime are accordingly suitable for the treatment of skin diseases which are accompanied by inflammation. It is known that preparations of this type can be used, for example, for the therapy of psoriasis, various forms of eczema, irritative and toxic dermatitis, UV dermatitis and further allergic and/or inflammatory diseases of the skin and integumentary appendages. Preparations according to the invention which, in addition to the compound of the formula I, additionally comprise an aryl oxime, preferably 2-hydroxy-5-methyl-laurophenone oxime, exhibit surprising antiinflammatory suitability.

30

The preparations here preferably comprise from 0.01 to 10% by weight of the aryl oxime, it being particularly preferred for the preparation to comprise from 0.05 to 5% by weight of aryl oxime.

5 All compounds or components which can be used in the preparations are either known or are commercially available or can be synthesised by known processes.

10 Besides the compounds described here, the preparations according to the invention may also comprise at least one photostabiliser, preferably conforming to the formula IV



where

$R^1$  is selected from  $-C(O)CH_3$ ,  $-CO_2R^3$ ,  $-C(O)NH_2$  and  $-C(O)N(R^4)_2$ ;

X is O or NH;

20  $R^2$  is a linear or branched  $C_{1-30}$ -alkyl radical;

$R^3$  is a linear or branched  $C_{1-20}$ -alkyl radical,

all  $R^4$ , independently of one another, are H or linear or branched  $C_{1-8}$ -alkyl radicals,

25  $R^5$  is H, a linear or branched  $C_{1-8}$ -alkyl radical or a linear or branched  $-O-C_{1-8}$ -alkyl radical, and

$R^6$  is a  $C_{1-8}$ -alkyl radical,

where the photostabiliser is particularly preferably bis(2-ethylhexyl) 2-(4-hydroxy-3,5-dimethoxybenzylidene)malonate. Corresponding  
30 photostabilisers and their preparation and use are described in International Patent Application WO 03/007906, the disclosure content of

which expressly also belongs to the subject-matter of the present application.

5 The compositions according to the invention can be prepared by processes that are well known to the person skilled in the art, in particular by the processes that serve for the preparation of oil-in-water emulsions or water-in-oil emulsions.

10 The present invention furthermore relates to preparations having antimicrobial properties comprising the antimicrobial pigments according to the invention and one or more cosmetically or dermatologically suitable vehicles, to a process for the production of a preparation which is characterised in that at least one antimicrobial pigment according to the invention is mixed with a cosmetically or dermatologically suitable vehicle,  
15 and to the use of antimicrobial pigments according to the invention for the production of a preparation having antimicrobial properties.

These compositions can be, in particular, in the form of simple or complex emulsions (O/W, W/O, O/W/O or W/O/W), such as creams, milks, gels, or  
20 gel-creams, powders and solid sticks, and they may, if desired, be formulated as aerosols and be in the form of foams or sprays.

The cosmetic compositions according to the invention can be used as compositions for protection of the human epidermis or of the hair against UV  
25 radiation, as sunscreens or make-up products.

It should be pointed out that in the formulations according to the invention for sun protection which have a vehicle of the oil-in-water emulsion type, the aqueous phase (which comprises, in particular, the hydrophilic filters)  
30 generally makes up from 50 to 95% by weight and preferably from 70 to 90% by weight, based on the formulation as a whole, the oil phase (which comprises, in particular, the lipophilic filters) makes up from 5 to 50% by

weight and preferably from 10 to 30% by weight, based on the formulation as a whole, and the (co)emulsifier or (co)emulsifiers make(s) up from 0.5 to 20% by weight and preferably from 2 to 10% by weight, based on the formulation as a whole.

5

For example, the one or more compounds of the formula I can be incorporated into cosmetic or dermatological preparations in the customary manner. Suitable preparations are those for external use, for example in the form of a cream, lotion or gel or as a solution that can be sprayed onto the skin. Suitable for internal use are administration forms such as capsules, coated tablets, powders, tablet solutions or solutions.

10

Examples which may be mentioned of application forms of the preparations according to the invention are: solutions, suspensions, emulsions, PIT emulsions, pastes, ointments, gels, creams, lotions, powders, soaps, surfactant-containing cleansing preparations, oils, aerosols and sprays. Examples of other application forms are sticks, shampoos and shower preparations. Any desired customary excipients, auxiliaries and, if desired, further active ingredients may be added to the preparation.

15

20

Preferred auxiliaries originate from the group consisting of preservatives, antioxidants, stabilisers, solubilisers, vitamins, colorants and odour improvers.

25

Ointments, pastes, creams and gels may comprise the customary excipients, for example animal and vegetable fats, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silica, talc and zinc oxide, or mixtures of these substances.

30

Powders and sprays may comprise the customary excipients, for example lactose, talc, silica, aluminium hydroxide, calcium silicate and polyamide powder, or mixtures of these substances. Sprays may additionally comprise

the customary propellants, for example chlorofluorocarbons, propane/butane or dimethyl ether.

5 Solutions and emulsions may comprise the customary excipients, such as solvents, solubilisers and emulsifiers, for example water, ethanol, isopropanol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butyl glycol, oils, in particular cottonseed oil, peanut oil, wheatgerm oil, olive oil, castor oil and sesame oil, glycerol fatty acid esters, polyethylene glycols and fatty acid esters of sorbitan, or mixtures of  
10 these substances.

Suspensions may comprise the customary excipients, such as liquid diluents, for example water, ethanol or propylene glycol, suspending agents, for example ethoxylated isostearyl alcohols, polyoxyethylene sorbitol esters  
15 and polyoxyethylene sorbitan esters, microcrystalline cellulose, aluminium metahydroxide, bentonite, agar-agar and tragacanth, or mixtures of these substances.

Soaps may comprise the customary excipients, such as alkali metal salts of  
20 fatty acids, salts of fatty acid monoesters, fatty acid protein hydrolysates, isethionates, lanolin, fatty alcohol, vegetable oils, plant extracts, glycerol, sugars, or mixtures of these substances.

Surfactant-containing cleansing products can comprise the conventional  
25 carriers, such as salts of fatty alcohol sulfates, fatty alcohol ether sulfates, sulfosuccinic acid monoesters, fatty acid albumen hydrolysates, isothionates, imidazolinium derivatives, methyl taurates, sarcosinates, fatty acid amide ether sulfates, alkylamidobetaines, fatty alcohols, fatty acid glycerides, fatty acid diethanolamides, vegetable and synthetic oils, lanolin  
30 derivatives, ethoxylated glycerol fatty acid esters or mixtures of these substances.

Face and body oils may comprise the customary excipients, such as synthetic oils, such as fatty acid esters, fatty alcohols, silicone oils, natural oils, such as vegetable oils and oily plant extracts, paraffin oils or lanolin oils, or mixtures of these substances.

5

Further typical cosmetic application forms are also lipsticks, lip-care sticks, mascara, eyeliner, eye-shadow, rouge, powder make-up, emulsion make-up and wax make-up, and sunscreen, pre-sun and after-sun preparations.

10 The preferred preparation forms according to the invention include, in particular, emulsions.

Emulsions according to the invention are advantageous and comprise, for example, the said fats, oils, waxes and other fatty substances, as well as  
15 water and an emulsifier, as usually used for a preparation of this type.

The lipid phase may advantageously be selected from the following group of substances:

- 20
- mineral oils, mineral waxes;
  - oils, such as triglycerides of capric or caprylic acid, furthermore natural oils, such as, for example, castor oil;
  - fats, waxes and other natural and synthetic fatty substances, preferably esters of fatty acids with alcohols having a low carbon number, for  
25 example with isopropanol, propylene glycol or glycerol, or esters of fatty alcohols with alkanoic acids having a low carbon number or with fatty acids;
  - silicone oils, such as dimethylpolysiloxanes, diethylpolysiloxanes, diphenylpolysiloxanes and mixed forms thereof.

30

For the purposes of the present invention, the oil phase of the emulsions, oleogels or hydrodispersions or lipodispersions is advantageously selected

from the group consisting of esters of saturated and/or unsaturated, branched and/or unbranched alkanecarboxylic acids having a chain length of from 3 to 30 carbon atoms and saturated and/or unsaturated, branched and/or unbranched alcohols having a chain length of from 3 to 30 carbon atoms, or from the group consisting of esters of aromatic carboxylic acids and saturated and/or unsaturated, branched and/or unbranched alcohols having a chain length of from 3 to 30 carbon atoms. Ester oils of this type can then advantageously be selected from the group consisting of isopropyl myristate, isopropyl palmitate, isopropyl stearate, isopropyl oleate, n-butyl stearate, n-hexyl laurate, n-decyl oleate, isooctyl stearate, isononyl stearate, isononyl isononanoate, 2-ethylhexyl palmitate, 2-ethylhexyl laurate, 2-hexyldecyl stearate, 2-octyldodecyl palmitate, oleyl oleate, oleyl erucate, erucyl oleate, erucyl erucate and synthetic, semi-synthetic and natural mixtures of esters of this type, for example jojoba oil.

15

The oil phase may furthermore advantageously be selected from the group consisting of branched and unbranched hydrocarbons and waxes, silicone oils, dialkyl ethers, or the group consisting of saturated and unsaturated, branched and unbranched alcohols, and fatty acid triglycerides, specifically the triglycerol esters of saturated and/or unsaturated, branched and/or unbranched alkanecarboxylic acids having a chain length of from 8 to 24, in particular 12-18, carbon atoms. The fatty acid triglycerides may advantageously be selected, for example, from the group consisting of synthetic, semi-synthetic and natural oils, for example olive oil, sunflower oil, soya oil, peanut oil, rapeseed oil, almond oil, palm oil, coconut oil, palm kernel oil and the like.

25

Any desired mixtures of oil and wax components of this type may also advantageously be employed for the purposes of the present invention. It may also be advantageous to employ waxes, for example cetyl palmitate, as the only lipid component of the oil phase.

30

The oil phase is advantageously selected from the group consisting of 2-ethylhexyl isostearate, octyldodecanol, isotridecyl isononanoate, iso-eicosane, 2-ethylhexyl cocoate, C<sub>12-15</sub>-alkyl benzoate, caprylic/capric acid triglyceride and dicapryl ether.

5

Particularly advantageous are mixtures of C<sub>12-15</sub>-alkyl benzoate and 2-ethylhexyl isostearate, mixtures of C<sub>12-15</sub>-alkyl benzoate and isotridecyl isononanoate, as well as mixtures of C<sub>12-15</sub>-alkyl benzoate, 2-ethylhexyl isostearate and isotridecyl isononanoate.

10

Of the hydrocarbons, paraffin oil, squalane and squalene may advantageously be used for the purposes of the present invention.

15

Furthermore, the oil phase may also advantageously have a content of cyclic or linear silicone oils or consist entirely of oils of this type, although it is preferred to use an additional content of other oil-phase components in addition to the silicone oil or the silicone oils.

20

The silicone oil to be used in accordance with the invention is advantageously cyclomethicone (octamethylcyclotetrasiloxane). However, it is also advantageous for the purposes of the present invention to use other silicone oils, for example hexamethylcyclotrisiloxane, polydimethylsiloxane or poly(methylphenylsiloxane).

25

Also particularly advantageous are mixtures of cyclomethicone and isotridecyl isononanoate and of cyclomethicone and 2-ethylhexyl isostearate.

30

The aqueous phase of the preparations according to the invention optionally advantageously comprises alcohols, diols or polyols having a low carbon number, and ethers thereof, preferably ethanol, isopropanol, propylene glycol, glycerol, ethylene glycol, ethylene glycol monoethyl or monobutyl ether, propylene glycol monomethyl, monoethyl or monobutyl ether,



diethylene glycol monomethyl or monoethyl ether and analogous products, furthermore alcohols having a low carbon number, for example ethanol, isopropanol, 1,2-propanediol or glycerol, and, in particular, one or more thickeners, which may advantageously be selected from the group consisting of silicon dioxide, aluminium silicates, polysaccharides and derivatives thereof, for example hyaluronic acid, xanthan gum, hydroxypropyl-methylcellulose, particularly advantageously from the group consisting of the polyacrylates, preferably a polyacrylate from the group consisting of the so-called Carbopols, for example Carbopol grades 980, 981, 1382, 2984 or 5984, in each case individually or in combination.

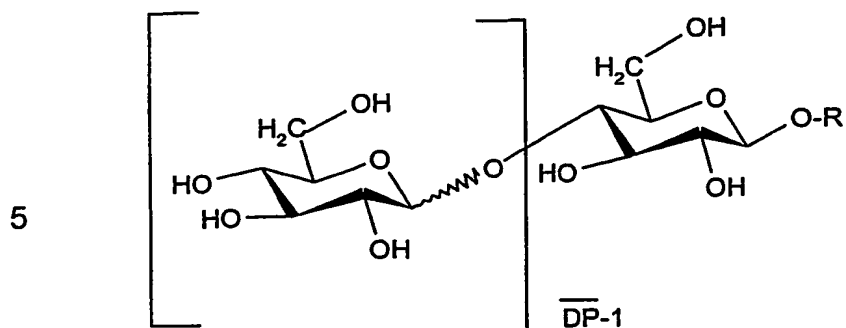
In particular, mixtures of the above-mentioned solvents are used. In the case of alcoholic solvents, water may be a further constituent.

Emulsions according to the invention are advantageous and comprise, for example, the said fats, oils, waxes and other fatty substances, as well as water and an emulsifier, as usually used for a formulation of this type.

In a preferred embodiment, the preparations according to the invention comprise hydrophilic surfactants.

The hydrophilic surfactants are preferably selected from the group consisting of the alkylglucosides, acyl lactylates, betaines and coconut ampho-acetates.

The alkylglucosides are themselves advantageously selected from the group consisting of the alkylglucosides which are distinguished by the structural formula



10 where R is a branched or unbranched alkyl radical having from 4 to 24 carbon atoms, and where  $\overline{DP}$  denotes a mean degree of glucosylation of up to 2.

15 The value  $\overline{DP}$  represents the degree of glucosidation of the alkylglucosides used in accordance with the invention and is defined as

$$\overline{DP} = \frac{p_1}{100} \cdot 1 + \frac{p_2}{100} \cdot 2 + \frac{p_3}{100} \cdot 3 + \dots = \sum \frac{p_i}{100} \cdot i$$

20 in which  $p_1, p_2, p_3 \dots p_i$  represent the proportion of mono-, di-, tri- ... i-fold glucosylated products in per cent by weight. Advantageous according to the invention are products having degrees of glucosylation of 1-2, particularly advantageously of from 1.1 to 1.5, very particularly advantageously of 1.2-1.4, in particular of 1.3.

25 The value DP takes into account the fact that alkylglucosides are generally, as a consequence of their preparation, in the form of mixtures of mono- and oligoglucosides. A relatively high content of monoglucosides, typically in the order of 40-70% by weight, is advantageous in accordance with the invention.

30

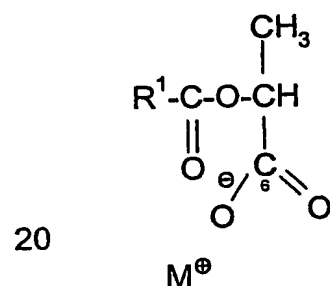
- 83 -

Alkylglycosides which are particularly advantageously used for the purposes of the invention are selected from the group consisting of octyl glucopyranoside, nonyl glucopyranoside, decyl glucopyranoside, undecyl glucopyranoside, dodecyl glucopyranoside, tetradecyl glucopyranoside and hexadecyl glucopyranoside.

It is likewise advantageous to employ natural or synthetic raw materials and auxiliaries or mixtures which are distinguished by an effective content of the active ingredients used in accordance with the invention, for example Plantaren<sup>®</sup> 1200 (Henkel KGaA), Oramix<sup>®</sup> NS 10 (Seppic).

The acyllactylates are themselves advantageously selected from the group consisting of the substances which are distinguished by the structural formula

15



20

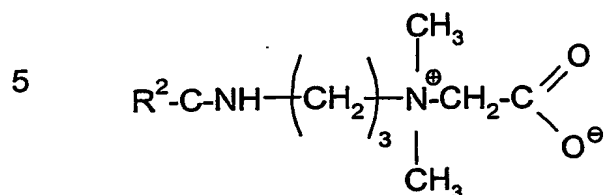
where R<sup>1</sup> is a branched or unbranched alkyl radical having from 1 to 30 carbon atoms, and M<sup>+</sup> is selected from the group consisting of the alkali metal ions and the group consisting of ammonium ions which are substituted by one or more alkyl and/or one or more hydroxyalkyl radicals, or corresponds to half an equivalent of an alkaline earth metal ion.

25

For example, sodium isostearyl lactylate, for example the product Pathionic<sup>®</sup> ISL from the American Ingredients Company, is advantageous.

30

The betaines are advantageously selected from the group consisting of the substances which are distinguished by the structural formula



where R<sup>2</sup> is a branched or unbranched alkyl radical having from 1 to 30 carbon atoms.

10

R<sup>2</sup> is particularly advantageously a branched or unbranched alkyl radical having from 6 to 12 carbon atoms.

15

For example, capramidopropylbetaine, for example the product Tego<sup>®</sup> Betain 810 from Th. Goldschmidt AG, is advantageous.

20

A coconut amphoacetate which is advantageous for the purposes of the invention is, for example, sodium coconut amphoacetate, as available under the name Miranol<sup>®</sup> Ultra C32 from Miranol Chemical Corp.

25

The preparations according to the invention are advantageously characterised in that the hydrophilic surfactant(s) is (are) present in concentrations of 0.01-20% by weight, preferably 0.05-10% by weight, particularly preferably 0.1-5% by weight, in each case based on the total weight of the composition.

30

For use, the cosmetic and dermatological preparations according to the invention are applied to the skin and/or the hair in an adequate amount in the usual manner for cosmetics.

Cosmetic and dermatological preparations according to the invention may exist in various forms. Thus, they may be, for example, a solution, a water-free preparation, an emulsion or microemulsion of the water-in-oil (W/O) or oil-in-water (O/W) type, a multiple emulsion, for example of the water-in-oil-in-water (W/O/W) type, a gel, a solid stick, an ointment or an aerosol. It is also advantageous to administer ectoins in encapsulated form, for example in collagen matrices and other conventional encapsulation materials, for example as cellulose encapsulations, in gelatine, wax matrices or liposomally encapsulated. In particular, wax matrices, as described in DE-A 43 08 282, have proven favourable. Preference is given to emulsions. O/W emulsions are particularly preferred. Emulsions, W/O emulsions and O/W emulsions are obtainable in a conventional manner.

Emulsifiers that can be used are, for example, the known W/O and O/W emulsifiers. It is advantageous to use further conventional co-emulsifiers in the preferred O/W emulsions according to the invention. The commercially available product Ceralution C (Sasol) has to be proven to be in particular advantageous as emulsifier.

Co-emulsifiers which are advantageous according to the invention are, for example, O/W emulsifiers, principally from the group consisting of the substances having HLB values of 11-16, very particularly advantageously having HLB values of 14.5-15.5, so long as the O/W emulsifiers have saturated radicals R and R'. If the O/W emulsifiers have unsaturated radicals R and/or R' or in the case of isoalkyl derivatives, the preferred HLB value of such emulsifiers may also be lower or higher.

It is advantageous to select the fatty alcohol ethoxylates from the group consisting of ethoxylated stearyl alcohols, cetyl alcohols, cetylstearyl alcohols (cetearyl alcohols). Particular preference is given to the following: polyethylene glycol (13) stearyl ether (steareth-13), polyethylene glycol (14) stearyl ether (steareth-14), polyethylene glycol (15) stearyl ether (steareth-

15), polyethylene glycol (16) stearyl ether (steareth-16), polyethylene glycol  
(17) stearyl ether (steareth-17), polyethylene glycol (18) stearyl ether  
(steareth-18), polyethylene glycol (19) stearyl ether (steareth-19),  
polyethylene glycol (20) stearyl ether (steareth-20), polyethylene glycol (12)  
5 isostearyl ether (isosteareth-12), polyethylene glycol (13) isostearyl ether  
(isosteareth-13), polyethylene glycol (14) isostearyl ether (isosteareth-14),  
polyethylene glycol (15) isostearyl ether (isosteareth-15), polyethylene  
glycol (16) isostearyl ether (isosteareth-16), polyethylene glycol (17)  
isostearyl ether (isosteareth-17), polyethylene glycol (18) isostearyl ether  
10 (isosteareth-18), polyethylene glycol (19) isostearyl ether (isosteareth-19),  
polyethylene glycol (20) isostearyl ether (isosteareth-20), polyethylene  
glycol (13) cetyl ether (ceteth-13), polyethylene glycol (14) cetyl ether  
(ceteth-14), polyethylene glycol (15) cetyl ether (ceteth-15), polyethylene  
glycol (16) cetyl ether (ceteth-16), polyethylene glycol (17) cetyl ether  
15 (ceteth-17), polyethylene glycol (18) cetyl ether (ceteth-18), polyethylene  
glycol (19) cetyl ether (ceteth-19), polyethylene glycol (20) cetyl ether  
(ceteth-20), polyethylene glycol (13) isocetyl ether (isoceteth-13),  
polyethylene glycol (14) isocetyl ether (isoceteth-14), polyethylene glycol  
(15) isocetyl ether (isoceteth-15), polyethylene glycol (16) isocetyl ether  
20 (isoceteth-16), polyethylene glycol (17) isocetyl ether (isoceteth-17),  
polyethylene glycol (18) isocetyl ether (isoceteth-18), polyethylene glycol  
(19) isocetyl ether (isoceteth-19), polyethylene glycol (20) isocetyl ether  
(isoceteth-20), polyethylene glycol (12) oleyl ether (oleth-12), polyethylene  
glycol (13) oleyl ether (oleth-13), polyethylene glycol (14) oleyl ether (oleth-  
25 14), polyethylene glycol (15) oleyl ether (oleth-15), polyethylene glycol (12)  
lauryl ether (laureth-12), polyethylene glycol (12) isolauryl ether (isolaureth-  
12), polyethylene glycol (13) cetylstearyl ether (cetareth-13), polyethylene  
glycol (14) cetylstearyl ether (cetareth-14), polyethylene glycol (15)  
cetylstearyl ether (cetareth-15), polyethylene glycol (16) cetylstearyl ether  
30 (cetareth-16), polyethylene glycol (17) cetylstearyl ether (cetareth-17),  
polyethylene glycol (18) cetylstearyl ether (cetareth-18), polyethylene

- 87 -

glycol (19) cetylstearyl ether (cetareth-19), polyethylene glycol (20) cetylstearyl ether (cetareth-20).

5 It is furthermore advantageous to select the fatty acid ethoxylates from the following group:

polyethylene glycol (20) stearate, polyethylene glycol (21) stearate, polyethylene glycol (22) stearate, polyethylene glycol (23) stearate, polyethylene glycol (24) stearate, polyethylene glycol (25) stearate, polyethylene glycol (12) isostearate, polyethylene glycol (13) isostearate, polyethylene glycol (14) isostearate, polyethylene glycol (15) isostearate, polyethylene glycol (16) isostearate, polyethylene glycol (17) isostearate, polyethylene glycol (18) isostearate, polyethylene glycol (19) isostearate, polyethylene glycol (20) isostearate, polyethylene glycol (21) isostearate, polyethylene glycol (22) isostearate, polyethylene glycol (23) isostearate, polyethylene glycol (24) isostearate, polyethylene glycol (25) isostearate, polyethylene glycol (12) oleate, polyethylene glycol (13) oleate, polyethylene glycol (14) oleate, polyethylene glycol (15) oleate, polyethylene glycol (16) oleate, polyethylene glycol (17) oleate, polyethylene glycol (18) oleate, polyethylene glycol (19) oleate, polyethylene glycol (20) oleate.

25 The ethoxylated alkyl ether carboxylic acid or salt thereof used can advantageously be sodium laureth-11 carboxylate. An alkyl ether sulfate which can advantageously be used is sodium laureth-14 sulfate. An ethoxylated cholesterol derivative which can advantageously be used is polyethylene glycol (30) cholesteryl ether. Polyethylene glycol (25) soyasterol has also proven successful. Ethoxylated triglycerides, which can advantageously be used, are the polyethylene glycol (60) evening primrose glycerides.

30 It is furthermore advantageous to select the polyethylene glycol glycerol fatty acid esters from the group consisting of polyethylene glycol (20) glyceryl laurate, polyethylene glycol (21) glyceryl laurate, polyethylene glycol

(22) glyceryl laurate, polyethylene glycol (23) glyceryl laurate, polyethylene glycol (6) glyceryl caprate/caprinic, polyethylene glycol (20) glyceryl oleate, polyethylene glycol (20) glyceryl isostearate, polyethylene glycol (18) glyceryl oleate/cocotate.

5

It is likewise favourable to select the sorbitan esters from the group consisting of polyethylene glycol (20) sorbitan monolaurate, polyethylene glycol (20) sorbitan monostearate, polyethylene glycol (20) sorbitan mono-isostearate, polyethylene glycol (20) sorbitan monopalmitate, polyethylene glycol (20) sorbitan monooleate.

10

Optional W/O emulsifiers, but ones which may nevertheless be advantageous for the purposes of the invention are the following:

15 fatty alcohols having from 8 to 30 carbon atoms, monoglycerol esters of saturated and/or unsaturated, branched and/or unbranched alkanecarboxylic acids having a chain length of from 8 to 24 carbon atoms, in particular 12-18 carbon atoms, diglycerol esters of saturated and/or unsaturated, branched and/or unbranched alkanecarboxylic acids having a chain length of from 8 to 24 carbon atoms, in particular 12-18 carbon atoms, monoglycerol ethers of saturated and/or unsaturated, branched and/or unbranched alcohols having a chain length of from 8 to 24 carbon atoms, in particular 12-18 carbon atoms, diglycerol ethers of saturated and/or unsaturated, branched and/or unbranched alcohols having a chain length of from 8 to 24 carbon atoms, in particular 12-18 carbon atoms, propylene glycol esters of saturated and/or unsaturated, branched and/or unbranched alkanecarboxylic acids having a chain length of from 8 to 24 carbon atoms, in particular 12-18 carbon atoms, and sorbitan esters of saturated and/or unsaturated, branched and/or unbranched alkanecarboxylic acids having a chain length of from 8 to 24 carbon atoms, in particular 12-18 carbon atoms.

25

30



Particularly advantageous W/O emulsifiers are glyceryl monostearate, glyceryl monoisostearate, glyceryl monomyristate, glyceryl monooleate, diglyceryl monostearate, diglyceryl monoisostearate, propylene glycol monostearate, propylene glycol monoisostearate, propylene glycol monocaprylate, propylene glycol monolaurate, sorbitan monoisostearate, sorbitan monolaurate, sorbitan monocaprylate, sorbitan monoisooleate, sucrose distearate, cetyl alcohol, stearyl alcohol, arachidyl alcohol, behenyl alcohol, isobehenyl alcohol, selachyl alcohol, chimyl alcohol, polyethylene glycol (2) stearyl ether (steareth-2), glyceryl monolaurate, glyceryl monocaprylate and glyceryl monocaprylate.

The preferred preparations according to the invention are particularly suitable for protecting human skin against ageing processes and against oxidative stress, i.e. against damage caused by free radicals, as are produced, for example, by solar irradiation, heat or other influences. In this connection, it is in the various administration forms usually used for this application. For example, it may, in particular, be in the form of a lotion or emulsion, such as in the form of a cream or milk (O/W, W/O, O/W/O, W/O/W), in the form of oily-alcoholic, oily-aqueous or aqueous-alcoholic gels or solutions, in the form of solid sticks or may be formulated as an aerosol.

The preparation may comprise cosmetic adjuvants which are usually used in this type of preparation, such as, for example, thickeners, softeners, moisturisers, surface-active agents, emulsifiers, preservatives, antifoams, perfumes, waxes, lanolin, propellants, dyes and/or pigments which colour the composition itself or the skin, and other ingredients usually used in cosmetics.

The dispersant or solubiliser used can be an oil, wax or other fatty substance, a lower monoalcohol or lower polyol or mixtures thereof. Particu-

larly preferred monoalcohols or polyols include ethanol, isopropanol, propylene glycol, glycerol and sorbitol.

5 A preferred embodiment of the invention is an emulsion in the form of a protective cream or milk which, apart from the compound(s) of the formula I, comprises, for example, fatty alcohols, fatty acids, fatty acid esters, in particular triglycerides of fatty acids, lanolin, natural and synthetic oils or waxes and emulsifiers in the presence of water.

10 Further preferred embodiments are oily lotions based on natural or synthetic oils and waxes, lanolin, fatty acid esters, in particular triglycerides of fatty acids, or oily-alcoholic lotions based on a lower alcohol, such as ethanol, or a glycerol, such as propylene glycol, and/or a polyol, such as glycerol, and oils, waxes and fatty acid esters, such as triglycerides of fatty acids.

15 The preparation according to the invention may also be in the form of an alcoholic gel which comprises one or more lower alcohols or polyols, such as ethanol, propylene glycol or glycerol, and a thickener, such as siliceous earth. The oily-alcoholic gels also comprise natural or synthetic oil or wax.

20 The solid sticks consist of natural or synthetic waxes and oils, fatty alcohols, fatty acids, fatty acid esters, lanolin and other fatty substances.

25 If a preparation is formulated as an aerosol, the customary propellants, such as alkanes, fluoroalkanes and chlorofluoroalkanes, are generally used.

30 The cosmetic preparation may also be used to protect the hair against photochemical damage in order to prevent colour changes, bleaching or damage of a mechanical nature. In this case, a suitable formulation is in the form of a rinse-out shampoo, lotion, gel or emulsion, the preparation in question being applied before or after shampooing, before or after colour-

ing or bleaching or before or after permanent waving. It is also possible to select a preparation in the form of a lotion or gel for styling or treating the hair, in the form of a lotion or gel for brushing or blow-waving, in the form of a hair lacquer, permanent waving composition, colorant or bleach for the hair. Besides the compounds of the formula I, the preparation having light-protection properties may comprise various adjuvants used in this type of composition, such as surfactants, thickeners, polymers, softeners, preservatives, foam stabilisers, electrolytes, organic solvents, silicone derivatives, oils, waxes, antigrease agents, dyes and/or pigments which colour the composition itself or the hair, or other ingredients usually used for hair care.

The entire disclosure of all applications, patents and publications, cited above are hereby incorporated by reference.

The pigments and their production process according to the present invention is more illustratively demonstrated but not limited by means of the following examples.

## Examples:

### L, a and b measurement:

The L, a and b values of the employed inorganic pigments and the antimicrobial pigments have been measured with a Phyma WICO 5&5 and a Minolta CR300 measurement system.

### Example 1:

#### ***Ronaspheres<sup>®</sup> treated with Ag<sub>2</sub>O***

30 g Ronaspheres<sup>®</sup> (D<sub>50</sub> 2.5-3.5μm, silica) are homogenised with 0.02% Ag<sub>2</sub>O by weight, based on the Ronaspheres<sup>®</sup>. Then 31 ml of distilled water are added to the mixture that is then stirred for 16 h. The reaction

temperature is held at 37°C. The initial dark colour of the reaction mixture turns to colourless at the end of the reaction indicating complete conversion of silver oxide. The suspension is filtered off and then washed several times with water and with acetone. The solvent is removed by evaporation and the pigments are then dried.

Visual comparison between the Ronaspheres<sup>®</sup> and the Ronaspheres<sup>®</sup> + 0.02% Ag<sub>2</sub>O do not show any noticeable change in colour.

L,a,b powder measurements:

L, a and b values:

of the employed inorganic pigment: L = 93.5; a = -0.2; b = +0.7

of the antimicrobial pigment: L = 93.6; a = -0.2; b = +0.9

15

### **Example 2:**

#### ***Timiron<sup>®</sup> pigments treated with Ag<sub>2</sub>O:***

5 g Timiron<sup>®</sup> Silk Gold (TiO<sub>2</sub> coated mica) are homogenised with 0.02% Ag<sub>2</sub>O by weight, based on the pigments. Then 11 ml of distilled water are added to the mixture that is then stirred for 16 h. The reaction temperature was held at 37°C. The initial dark colour of the reaction mixture turns to the original colour of the pigment during the reaction indicating complete conversion of silver oxide. The suspension is sucked off, and then washed several times with water and with acetone. The solvent is removed by evaporation and the pigments are then dried.

Visual comparison between the colour card of Timiron<sup>®</sup> Silk Gold and the colour card with Timiron<sup>®</sup> Silk Gold + 0.02% Ag<sub>2</sub>O do not show any noticeable change in colour.

L,a,b powder measurements:

L, a and b values:

of the employed inorganic pigment: L = 88.3; a = -2.6; b = 10.5

of the antimicrobial pigment: L = 88.3; a = -2.5; b = 10.6

5

**Example 3:**

***Timiron® pigments treated with Ag<sub>2</sub>O:***

10 5 g Timiron® Starluster MP 115 (TiO<sub>2</sub> coated mica) are homogenised with  
0.02% Ag<sub>2</sub>O by weight, based on the pigments. Then 11 ml of distilled  
water are added to the mixture that is then stirred for 16 h. The reaction  
temperature was held at 37°C. The initial dark colour of the reaction  
mixture turns to the original colour of the pigment during the reaction  
15 indicating complete conversion of silver oxide. The suspension is sucked  
off, and then washed several times with water and with acetone. The  
solvent is removed by evaporation and the pigments are then dried.

20 Visual comparison between the colour card of Timiron® Starluster MP 115  
and the colour card with Timiron® Starluster MP 115 + 0.02% Ag<sub>2</sub>O do not  
show any noticeable change in colour.

L,a,b powder measurements:

L, a and b values of the employed inorganic pigment and the antimicrobial  
pigment (example 3):

25

of the employed inorganic pigment: L = 88.4; a = +0,4; b = +3,6

of the antimicrobial pigment: L = 88.3; a = +0,4; b = +3,7

**Example 4-5:**

30 Day creams (O/W) with antimicrobial Ronaspheres® (Example 1):

- 94 -

	<u>Example</u>		<u>4</u>	<u>5</u>
	Raw material	Manufacturer	[%]	[%]
	<b>A</b>			
	Ronasphere®+0.02%	(1)	5.00	1.00
	Ag <sub>2</sub> O	(2)	1.00	1.00
5	Veegum HV	(1)	3.00	3.00
	Karion F liquid		57.00	61.00
	Water, deionised			
	<b>B</b>			
	Arlacel 165 VP	(3)	5.00	5.00
	Lanette O	(4)	1.50	1.50
	Miglyol 812 N	(5)	7.00	7.00
10	Sheabutter solid	(6)	2.00	2.00
	Cetiol SN	(4)	7.00	7.00
	Eutanol G	(4)	7.50	7.50
	Emulgade PL 68/50	(4)	2.00	2.00
	<b>C</b>			
	Dow Corning 345	(7)	2.00	2.00
15	Total		100.00	100.00

**Manufacturers:**

- (1) Merck KGaA/Rona®
- (2) Vanderbilt
- (3) Uniqema
- 20 (4) Cognis GmbH
- 5) Sasol Germany GmbH
- (6) H. Erhard Wagner GmbH
- (7) Dow Corning

25

**Preparation:**

30

Veegum is dispersed in the water of phase A, adding resting raw materials and heating to 80°C. Adding phase B heated to 80°C into phase A, followed by homogenising. During cooling to 40°C the mixture is stirred. Afterwards phase C is added and the resulting mixture is cooled to room temperature and adjusted to pH 6.0.

**Examples 6-7:**

Body lotions with antimicrobial Timiron® Starluster (Example 3)

5	<b>Example</b>	<b>Raw material</b>	<b>Manufacturer</b>	<b>6</b> [%]	<b>7</b> [%]
	<b>A</b>				
		Timiron® Starluster +	(1)	5.00	1.00
		0.02% Ag <sub>2</sub> O			
		Carbopol ETD 2001	(2)	0.60	0.60
		Water, deionised		38.30	42.30
10	<b>B</b>				
		RonaCare® Allantoin	(1)	0.20	0.20
		Water, deionised		31.00	31.00
	<b>C</b>				
		Hostaphat KL 340 D	(3)	3.00	3.00
15		Cetylalkohol	(1)	2.00	2.00
		Paraffine liquid	(1)	10.05	10.05
		Cetiol V	(4)	6.00	6.00
	<b>D</b>				
		Triethanolamine	(1)	0.35	0.35
		Water, deionised		3.50	3.50
20		<b>Total</b>		<b>100.00</b>	<b>100.00</b>
	<b>Manufacturers:</b>				
	(1) Merck KGaA/Rona®				
	(2) Noveon				
	(3) Clariant GmbH				
25	(4) Cognis GmbH				

**Preparation:**

The pigment is dispersed in water of phase A. To lower the viscosity, citric acid can be added. Afterwards Carbopol is added. After complete solution the phase B is slowly added. Phase A/B and C are heated up to 80°C and phase C is stirred into phase A/B and homogenised. Then the mixture is

neutralised and homogenised with phase D. The mixture is cooled down during continuous stirring.

5

**Examples 8-9:**

Sparkling body creams with antimicrobial Timiron® Silk Gold (Example 2)

	<b>Example</b>		<b><u>8</u></b>	<b><u>9</u></b>
	<b>Raw material</b>	<b>Manufacturer</b>	<b>[%]</b>	<b>[%]</b>
10	<b>A</b>			
	Timiron® Silk Gold +	(1)	5.00	1.00
	0.02% Ag <sub>2</sub> O			
	Carbopol ETD 2001	(2)	0.60	0.60
	Water, deionised		38.30	42.30
	<b>B</b>			
15	RonaCare® Allantoin	(1)	0.20	0.20
	Water, deionised		31.00	31.00
	<b>C</b>			
	Hostaphat KL 340 D	(3)	3.00	3.00
	Cetylalkohol	(1)	2.00	2.00
	Paraffin flüssig	(1)	10.05	10.05
	Cetiol V	(4)	6.00	6.00
20	<b>D</b>			
	Triethanolamin	(1)	0.35	0.35
	Water, deionised		3.5	3.5
	<b>Total</b>		<b>100.00</b>	<b>100.00</b>

25

**Manufacturers:**

(1) Merck KGaA/Rona®

(2) Noveon

(3) Clariant GmbH

(4) Cognis GmbH

30

**Preparation:**



- 97 -

The pigment is dispersed in water of phase A. To lower the viscosity, citric acid can be added. Afterwards Carbopol is added with stirring. After complete solution the phase B is slowly added. Phase A/B and C are heated up to 80°C and phase C is stirred into phase A/B and homogenised. Then the mixture is neutralised and homogenised with phase D. The mixture is cooled down during continuous stirring.

**Example 10:**

10. Deodorant Lotion with antimicrobial Ronaspheres® (Example 1):

	Raw material	Manufacturer	[%]
	<b>A</b>		
	Glyceryl Stearate	(1)	3.1
	(and) Ceteth-20		
15	Cetearyl Octanoate	(1)	3.1
	Caprylic/Capric	(1)	3.1
	Triglyceride		
	Stearyl Alcohol	(1)	1.1
	Dimethicone	(1)	0.5
	<b>B</b>		
	Glycerin		3.0
20	Aqua		84.95
	Ronasphere® + 0.02%		1
	Ag <sub>2</sub> O		
	<b>C</b>		
	Citric Acid		0.15

25 **Manufacturers:**  
(1) Goldschmidt

**Preparation:**

Phase A and phase B are separately heated to 80°C. The phases are combined without stirring, thus avoiding the formation of an O/W emulsion.

- 98 -

The mixture is homogenised and cooled down to 30°C during stirring.

Phase C is added at temperatures below 40°C.

5      **Example 11:**

Deo-Roll-On with antimicrobial Timiron® Silk Gold (Example 2):

	Raw material	Manufacturer	%
10	<b>A</b>		
	Hydroxypropyl	(1)	1.2
	Methylcellulose		
	Aqua		86.4
15	<b>B</b>		
	Timiron® Silk Gold + 0.02%		0.5
	Ag <sub>2</sub> O		
	Glycolic Acid	(2)	0.04
	Aqua		9.86
	Glycerin		2.0

**Manufacturers:**

(1) Dow Corning

(2) Merck KGaA

20

**Preparation:**

25      The cellulose is slowly added to water during continuous stirring until a transparent and viscous swelling is obtained. Phase B is added to phase A and homogenously stirred.

**Example 12:**

30      Decorative Laminate Printing

- 99 -

guide recipe:

water based gravure printing

- 5
- 10% Colorstream® F10-00 Autumn Mystery
  - 3% Antimicrobial pigment of example 2
  - 43% protein binder
  - 15% ethanol
  - 30% water

10

**Example 13:**

Packaging Printing

guide recipe:

15 solvent based gravure printing

- 20% T10-01 Colorstream® Viola Fantasy
- 5% Antimicrobial pigment of example 3
- 75% nitrocellulose/ethanol binder

20

adjustment to print viscosity:

- 65% base ink (s.a.)
- 35% ethoxypropanol

25

**Example 14:**

Paper Coating

guide recipe:

direct application

30

- 3.6% Colorstream® T 10-01 Viola Fantasy

- 100 -

0.6% Antimicrobial pigment of example 2  
0.2% Pigment Green 7 (Flexiverse Green GFD 0701)  
0.2% Pigment Blue 15:3 (Flexiverse Blue BFD 1531)  
20.4% styrene/acrylate copolymer  
75% water

5

**Anti-microbial investigations:**

10

A standard procedure to measure the anti-microbial activity of substances was used (challenge tests). A suspension of test organisms ( $10^5$  to  $10^6$  germs/ml) is inoculated into a recipient containing already the substance to be tested. Samples of the inoculated suspension are taken and the number of germs is measured thanks to the Agar plates method. Germ counts is performed at  $t = 0$ ,  $t = 24\text{h}$  after the inoculation,  $t = 48\text{h}$  after the inoculation,  $t = 7\text{ days}$  after the inoculation,  $t = 14\text{ days}$  after the inoculation.

15

Sterile water containing 8% w/w of treated and untreated carriers were each investigated.

20

**Ronaspheres® of Example 1 in an 8% aqueous suspension**

25

Organism	Germs Number/ml after					
	Inoculum	Start	24h	48h	7d	14d
<b><u>Bacteria</u></b>						
Escheria coli ATCC8739	$3.1 \cdot 10^6$	$3.6 \cdot 10^6$	0	0	0	0
Pseudomonas	$8.5 \cdot 10^5$	$8.4 \cdot 10^5$	0	0	0	0

30

- 101 -

5	aeruginosa ATCC 9027					
	Staphylococcus aureus ATCC 6538	$3.7 \cdot 10^6$	$1.87 \cdot 10^6$	0	0	0
	<b><u>Yeast and Fungi</u></b>					
10	Candida albicans ATCC 10231	$7.8 \cdot 10^5$	$7.1 \cdot 10^5$	$1.4 \cdot 10^2$	0	0
	Aspergillus niger ATCC 16404	$5.0 \cdot 10^5$	$3.9 \cdot 10^5$	$1.3 \cdot 10^5$	0	0

**Blind value: 0,02% Ag<sub>2</sub>O in an 8% aqueous suspension**

15		Germs Number /ml after					
	Organism	Inoculum	Start	24h	48h	7d	14d
	<u>Bacteria</u>						
20	Escheria coli ATCC8739	$3.1 \cdot 10^6$	$2.0 \cdot 10^6$	0	0	0	0
	Pseudomonas aeruginosa ATCC 9027	$8.5 \cdot 10^5$	$2.2 \cdot 10^5$	0	0	0	0
	Staphylococcus aureus ATCC 6538	$3.7 \cdot 10^6$	$2.7 \cdot 10^6$	0	0		0
	<u>Yeast and Fungi</u>						
	Candida albicans ATCC 10231	$7.8 \cdot 10^5$	$9.0 \cdot 10^2$	$8.3 \cdot 10^2$	0	0	0
	Aspergillus niger ATCC 16404	$5.0 \cdot 10^5$	$4.5 \cdot 10^5$	$3.5 \cdot 10^5$	$1.6 \cdot 10^5$	$1.0 \cdot 10^5$	$2.2 \cdot 10^4$

**Ronaspheres® Blind value in an 8% aqueous suspension**

Ronaspheres® alone do not show any significant anti-microbial activity.

30

	Germs Number /ml after				
Organism	Inoculum	Start	24h	4d	7d

- 102 -

	<b><u>Bacteria</u></b>					
	Escheria coli ATCC8739	$3.2 \cdot 10^6$	$3.2 \cdot 10^6$	$3.8 \cdot 10^6$	$3.2 \cdot 10^6$	$6.9 \cdot 10^5$
5	Pseudomonas aeruginosa ATCC 9027	$1.7 \cdot 10^6$	$1.4 \cdot 10^6$	$2.1 \cdot 10^6$	$1.1 \cdot 10^6$	$8.9 \cdot 10^5$
	Staphylococcus aureus ATCC 6538	$2.0 \cdot 10^6$	$9.8 \cdot 10^5$	$3.8 \cdot 10^6$	$3.3 \cdot 10^5$	$6.9 \cdot 10^4$
	<b><u>Yeast and Fungi</u></b>					
10	Candida albicans ATCC 10231	$9.2 \cdot 10^5$	$7.2 \cdot 10^5$	$8.2 \cdot 10^5$	$8.0 \cdot 10^5$	$8.9 \cdot 10^5$
	Aspergillus niger ATCC 16404	$3.8 \cdot 10^5$	$8.3 \cdot 10^5$	$2.5 \cdot 10^5$	$3.8 \cdot 10^5$	$1.2 \cdot 10^5$

15

**Antimicrobial Timiron® Starluster (Example 3) in an 8% aqueous suspension**

7 days after the inoculation the whole amount of microorganisms were killed.

20

**Timiron® Starluster (Blind value) in an 8% aqueous suspension**

The pigment alone does not show any bactericide or fungicide activity.

25

**Antimicrobial Timiron® Silk Gold (Example 2) in an 8% aqueous suspension:**

7 days after the inoculation the whole amount of microorganisms were killed.

30

**Timiron® Silk Gold (Blind value) in an 8% aqueous suspension**

The pigment alone does not show any bactericide or fungicide activity.

**Timiron® Silk Gold + 0.01% Ag<sub>2</sub>O (preparation procedure similar to example 2) in a 8% aqueous suspension**

5		Germs Number /ml after					
	Organism	Inoculum	Start	24h	4d	7d	14d
	<b><u>Bacteria</u></b>						
	Escheria coli ATCC8739	$2.1 \cdot 10^6$	$3.9 \cdot 10^5$	0	0	0	0
10	Pseudomonas aeruginosa ATCC 9027	$1.6 \cdot 10^6$	$3.2 \cdot 10^5$	0	0	0	0
	Staphylococcus aureus ATCC 6538	$1.2 \cdot 10^6$	$1.3 \cdot 10^6$	$1,3 \cdot 10^3$	0	0	0
15	<b><u>Yeast and Fungi</u></b>						
	Candida albicans ATCC 10231	$8.6 \cdot 10^5$	$1.0 \cdot 10^5$	0	0	0	0
20	Aspergillus niger ATCC 16404	$3.8 \cdot 10^5$	$1.9 \cdot 10^5$	$5.8 \cdot 10^4$	$3.3 \cdot 10^4$	$6.9 \cdot 10^3$	$1.4 \cdot 10^3$

**Timiron® Starluster + 0,01% Ag<sub>2</sub>O (preparation procedure similar to example 3) in a 8% aqueous suspension**

25		Germs Number /ml after					
	Organism	Inoculum	Start	24h	4d	7d	14d
	<b><u>Bacteria</u></b>						
30	Escheria coli ATCC8739	$2.1 \cdot 10^6$	$5.4 \cdot 10^5$	$1.5 \cdot 10^3$	0	0	0
	Pseudomonas	$1.6 \cdot 10^6$	$7.1 \cdot 10^5$	0	0	0	0

5	aeruginosa ATCC 9027					
	Staphylococcus aureus ATCC 6538	$1.2 \cdot 10^6$	$1.7 \cdot 10^6$	$1.7 \cdot 10^4$	0	0
	<u><b>Yeast and Fungi</b></u>					
	Candida albicans ATCC 10231	$8.6 \cdot 10^5$	$3.2 \cdot 10^5$	$1.4 \cdot 10^2$	0	0
	Aspergillus niger ATCC 16404	$3.8 \cdot 10^5$	$2.5 \cdot 10^5$	$9.5 \cdot 10^4$	$6.5 \cdot 10^4$	$1.4 \cdot 10^4$
10						$3.7 \cdot 10^3$

15 **Determination of the bacteriostatic activity of the antimicrobial pigments (Minimal inhibitory concentrations (MIC)):**

20 The MICs were determined using an agar dilution method based on DIN 58940 and 58944. Petri dishes of 8.5 cm diameter were poured with 9 ml of freshly prepared Mueller-Hinton agar (Merck Company) or Wilkins-Chalgren agar (Oxoid, supplemented with 10 g Agar-agar per liter) maintained in liquid form at 50°C, to which the sample dilutions at various concentrations had been added at 25%. To prepare the sample dilutions, a 24.3% solution of the solid sample material was prepared with Aqua bidest.

25 Progressive 1:2 dilutions of this solution were made with Aqua bidest to prepare further test concentrations that were set up in the form of geometric series. 4-fold lower final concentrations were reached by additional dilution with the test agar. Two agar plates were poured for each test concentration and culture medium.

30 After solidification and drying, the test plates were inoculated with 1 µl drops of the test microbe suspensions. The agar plates were incubated and



- 105 -

subsequently evaluated. The MIC was given as the lowest concentration of the active substance at which there was no macroscopically visible growth.

The results are shown in the following tables:

5	<b>Acne application</b>	<b>MICs in water and in% for:</b>		
	<b>Pigments</b>	<b>Talc Low Coat/ 0.03% Ag<sub>2</sub>O</b>	<b>Micronaspheres/ 0.02% Ag<sub>2</sub>O</b>	<b>Mica Low Coat/0.07% Ag<sub>2</sub>O</b>
	<b>Germes</b>			
	<i>Propionibacterium acnes</i>	4.05	4.05	0.76
	<i>Staphylococcus epidermidis</i>	4.05	2.03	1.52
10	<b>Deodorant Application</b>			
	<i>Corynebacterium xerosis</i>	8.1	2.03	1.52
	<i>Staphylococcus aureus</i>	8.1	4.05	3.04
	<i>Staphylococcus epidermidis</i>	4.05	2.03	1.52

15

	<b>Oral Care</b>	<b>MICs in water and in% for:</b>	
	<b>Pigments</b>	<b>MP 149 / 0,02% Ag<sub>2</sub>O</b>	
	<b>Germes</b>		
	<i>Actinomyces viscosus</i>	>8.1	
	<i>Prevotella intermedia</i>	>8.1	
	<i>Fusobacterium nucleatum</i>	>8.1	
20	<i>Porphyromonas gingivalis</i>	>8.1	
	<i>Srepttococcus mutans</i>	8.1	
	<i>Streptococcus salivarius</i>	>8.1	
	<i>Streptococcus sanguinis</i>	4.05	
	<b>Dandruff</b>	<b>MP 115/0.02 % Ag<sub>2</sub>O</b>	<b>MP 1001/0.07 % Ag<sub>2</sub>O</b>
	<i>Malazessia furfur</i>	4.05	1.0

25

30